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AN INTERNATIONAL ENCYCLOPEDIA

OF

MODERN MEDICAL SCIENCE

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EDITED BY

THOMAS L. STEDMAN, M.D.
NEW YORK CITY

IN TWENTY VOLUMES

VOLUME XVIII

SYPHILIS AND LEPROSY

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CONTRIBUTORS TO VOLUME XVIII.

JONATHAN HUTCHINSON, M.D., LL.D., F.R.S., F.R.S.C., London.

Consulting Surgeon to the London Hospital; Senior Surgeon, Hospital for Diseases of the Skin, Blackfriars; Consulting Surgeon, Royal London Ophthalmic Hospital; Emeritus Professor of Surgery in the London Hospital Medical School.

EDUARD LANG, M.D., Vienna.

Professor of Dermatology and Syphilology, University of Vienna.

PRINCE A. MORROW, M.D., New York.

Professor of Genito-urinary Diseases in the University and Bellevue Hospital Medical College; Attending Physician to the Department of Skin and Venereal Diseases, New York Hospital; Surgeon to the City Hospital; Consulting Dermatologist to St. Vincent's Hospital.

ACQUIRED SYPHILIS.

BY

E. LANG,

VIENNA.

VOL. XVIII.—1

ACQUIRED SYPHILIS.

Definition.—We have every reason to look for a living organism in the syphilitic contagium; but as we have not as yet found it, we are unable to give a precise definition of syphilis. We must at present be satisfied to characterize the disease by enumerating the effects produced by the contagium—and this is the task to which we shall have to devote the greater part of the following study.

The Syphilitic Infection.

During a limited period the pathological products and many of the physiological elements of those affected by syphilis contain a fixed contagium, which, inoculated into a healthy person by accident or design, is capable of reproducing the disease. It seems that the contagium does not penetrate the intact epithelial layer of the skin or of the mucous membrane, but that an inoculation is effected only in parts deprived of epithelium or when the contagious principle is introduced beneath the epithelial layer. But it is reasonable to suppose that the contagium may also penetrate alongside of the roots of the hairs or into the opening of a follicle, and so gain entrance into the organism.

At the point of entrance of the specific virus—the point of infection—a typical local change develops, which is usually followed by general symptoms of a special character. This contagium then reproduces itself for many years within the diseased organism, and also retains its virulence for a period of time which cannot as yet be fixed accurately. During this period it is so far unchanged that, transferred to healthy persons, it may produce the same morbid symptoms.

The general disorders (constitutional syphilis) are manifested by a chain of symptoms continuing for years, sometimes for life. During this time there are periods of relative, apparently complete health, without anything abnormal being observed—the so-called "latent periods." In many cases, however, probably in most, syphilis dies out after a relatively short period.

The typical initial local changes produced by the syphilitic virus are rarely missing, but in some exceptional cases they cannot be found. Syphilitic semen, in producing conception, may at the same

time infect the woman and cause constitutional syphilis without the occurrence of an initial lesion, and the same is true as regards women who have become syphilitic during pregnancy by retroinfection from the fœtus. The initial symptoms are always absent if the virus is introduced with the generative cell, in which case the advance of the disease coincides with the development of the fœtus, and we encounter only general disorders without local lesion. This syphilis developing during intrauterine life is the inherited, hereditary, or congenital form, which differs from acquired syphilis in various other ways as well.

Whether or not the contagium of syphilis can be transferred to the second generation, appears to me to be as yet undetermined.

If the contagium penetrates the skin or the mucous membrane at a point where desquamation has occurred or where there is a chap or crack in the integument, an accidental or artificial injury, or an open follicle (?), then an infiltration occurs, constituting the initial syphilitic manifestation. But this does not occur, provided no other infectious material is inoculated at the same time, until after a symptomless period of days or weeks; and, furthermore, the lesion appears only at the point of infection.

This *incubation period* usually lasts two, three, or four weeks; occasionally, however, it has been observed to last only one week, sometimes five or six weeks, or even eight weeks (J. Hutchinson).

After the initial lesion has existed a few days, there arises a usually painless swelling of the nearest lymph bodies or those of the second remove—the indolent bubo, sclerosis of the glands, scleradenitis; at the same time we frequently enough see the lymphatic vessels between the initial lesion and the bubo changed into thick, knobby cords—sclerosis of the lymphatic vessels, sclerotic lymphangitis.

After a few more weeks—the so-called second incubation—there appear symptoms of general infection, which may involve any organ and any tissue, either singly or in combination. These symptoms may last, with brief or protracted interruptions (sometimes of years), for a variable period. This is general or constitutional syphilis, characterized by latent periods and relapses. Sometimes we see in this so-called second incubation—which I prefer to call the "intermediary stage"—at a variable period after the initial symptoms, the development of characteristic (intermediary) syphilitic lesions. These are either interjected prodromes of the general eruption, or they have to be considered as the result partly of regional active or passive migration of the contagium, and partly of accidental or intentional infection—postinitial infection.

In some accurately described cases of experimental infection of

syphilis, the intervals between the infection and the appearance of the initial symptoms (first incubation), and between this and the first symptom of general infection (second incubation), can be exactly determined. Thus the duration of the first incubation period was, minimum, ten days (in one case); maximum, forty-two days (in one case)—the average being between three and four weeks. That of the second incubation period was, minimum, between one and two weeks (once); maximum, one hundred and fifty-nine days (once)—average from six to twelve weeks. As we shall see later, it is not always easy to determine the moment of the general infection. Undoubtedly the character of the generalization makes some difference. It is therefore not a matter for surprise that clinical experience shows great variety in this respect.

PATHOLOGY.

Various pathological changes are effected in the tissues in consequence of the entrance and generalization of the specific virus in the body. Hyperæmia is very frequent, but is usually of short duration; if it does not disappear soon, there follows a slight degree of infiltration, which is to be regarded as a transition stage leading to a mild inflammatory process.

Like the hyperæmia, these inflammations of mild degree end in resolution, the infiltrate becoming absorbed and the original normal condition being reëstablished. Sometimes, however, the infiltrate assumes the form of a long-continued or even permanent enlargement of either connective tissue or bone, according to the location of the initial process. Occasionally, under certain conditions, we find a breaking down or suppuration in the infiltrated parts, and if these parts are superficial the resultant abscesses break through and form ulcers; or the disintegration begins on the surface and the infiltration leads immediately to ulceration, without abscess; but in both cases recovery without especial loss of substance is the usual result. These conditions are identical with those of simple congestion, inflammation, or hyperplasia, and are therefore regarded by Virchow as of irritative character. Histologically they differ but little from other inflammatory processes. We frequently see the elements of the blood-vessels prominently concerned in the process of proliferation, and this results in thickening of the walls of the vessels, and even narrowing or obliteration of their lumen.

Essentially different from these irritative processes is another series of processes caused by syphilis, most of which belong either to the gummata or to the syphilitic callosities.

Gumma is usually an infiltration which produces destruction of the

normal intermediate tissue, and which is either absorbed (with inevitable destruction of the tissue), or remains as a caseous thickening, or bursts and discharges the contents externally. Gumma appears either as a new formation from the size of a grain of wheat up to a large tumor, with sharply circumscribed outlines or with radiating processes, or as a diffuse infiltration. It forms a whitish to a reddish-gray soft mass, consisting of a tender, gelatinous, here and there fibrous, intercellular substance, with proliferated cells, which arise from connective tissue, or from the migrating elements of the smallest blood and lymphatic vessels, or from emigrated white blood cells; they look like granulation cells or colorless blood corpuscles, wherefore gummata have been classified by Virchow as granulation tumors, granulomata, and by Klebs as leucocytomata.

Besides these cells resembling white corpuscles, there are larger formations in a gumma, epithelioid forms, and some which look like giant cells. According to their histological composition, there is an undeniable analogy between gummata and the neoplasmata of glanders, pearl disease, tuberculosis (scrofula, lupus), and leprosy; and as the infectious nature of these diseases cannot be denied, these neoplasms may also be called "infectious tumors," as Klebs names them. Wagner, however, regards the gumma as a specific new formation, which he calls "syphiloma."

Although through the chronicity of its course the gumma is usually of long duration, nevertheless a limit to its existence is set by the fact of its inevitable disintegration. It disappears gradually in one of three different ways: either the cells forming the gumma become fatty degenerated, or they break up into a granular mass and are absorbed, or they increase in size and become confluent, forming the so-called giant cells, which also finally disintegrate and are absorbed. But as the gumma cells, after a long period, destroy also the original tissues between them, consisting of blood-vessels, muscle fibres, gland cells, etc., it follows that after the absorption of a rather chronic gumma, a portion of the parenchyma, in which the gumma was located, is also absorbed. The part where this loss of tissue has occurred shrinks, and in this way deformities of the most varied character are produced.

The fatty degenerated gumma may also become fluid and be transformed into a purulent mass, discharge externally, and so lead to the formation of an ulcer, which then cleans up and heals, leaving a scar after the necrotic parts have sloughed away and if no new infiltrations appear.

The gumma follows a different course, if, as happens frequently, a new formation of connective tissue occurs around it, and by a proc-

ess of gradual shrinking forms a hard mass. The gumma is inside of this fibrous mass, and its absorption is thereby often rendered difficult. The disintegrated constituents of the gumma thicken into a fatty, granular mass, with destroyed cells and nuclei, assume a cheesy character, and either remain as inorganic matter, or the caseous mass, like a foreign body, excites inflammation and suppuration, as a result of which it is finally cast out, leaving an ulcer with indurated borders.

The gumma is thus a cellular new growth, the elements of which assume at one period a grouping similar to that of a tumor; but the tumorous character corresponds only to one phase of the gumma, which usually does not become organized, but eventually heals through either absorption or ulceration, or else thickens finally into a dry cheesy mass. I think it is better for clinicians to regard gumma as a chronic inflammatory process.

The tumor-like character of the gumma is absent when it is produced very slowly by an infitration, the elements of which are not massed in great numbers, but are found rather spread out over a broad superficial area. Such gummatous infiltrations also often lead to a new formation of connective tissue in the neighborhood, which slowly thickens and assumes in the soft parts the form of a fibrous, cicatricial, often contracting body. This product, in which the gumma is thrust into the background, represents the syphilitic induration *par excellence*. It appears under the microscope as a dense connective-tissue mass, in the fibres of which we find, according to the time of our examination, more or less numerous young cells, or such as have already undergone fatty degeneration (as in the gumma). In the bones an analogous process leads to sclerosis.

Syphilitic induration and gumma, however, often combine in various ways, sometimes the one prevailing, sometimes the other.

We have not as yet succeeded in obtaining a perfect understanding of the mutual relations of the various pathological processes which appear during the course of syphilis, probably because we have not yet acquired a clear knowledge of the character of the syphilitic contagium. According to the present state of science we must suppose the syphilitic contagium to be a living organism, which has the faculty of multiplying in healthy individuals. I advanced this view as early as the year 1871, on the occasion of my inaugural address when appointed professor at the University of Vienna, and endeavored at that time to prove, by the clinical course of syphilis and by certain special properties of the contagium, the following conclusions: The contagium, coming from the point of infection, gaining entrance into the circulation, probably by way of the lymph channels, is taken

by the blood to all the various tissues, whereby some mostly trivial and harmless changes are effected—irritative conditions. Gradually the virulence of the contagium deposited in the tissues diminishes, but it still possesses the property of exciting new disorders of similar nature, as the result of some as yet unknown influences, *i.e.*, to produce relapses. Later the contagium loses entirely its destructive quality, when we have perfect recovery; or partially only, when we have merely improvement. In these cases the contagium undergoes the further change that it loses in a certain, so far unknown time the power to propagate the disease in healthy persons—that is to say, it loses the power of infection. Although it would be highly important for the practitioner to know this time exactly in certain cases, it is as yet impossible. The supposition that the danger of infection ceases after syphilis has lasted for two, three, or four years, is based upon very insecure premises; and although the disease does usually die out after a few years, cases occur (rarely it is true) in which a syphilitic person infects a healthy one after six, ten, or even more years. But even if the poison loses its power of infection, it may remain latent, until by some often external cause it is stimulated to new growth and produces in a definite part a very characteristic reaction, which represents the late form of syphilis; the semicircular and circular (serpiginous) forms of the later syphilitic manifestations justify the conclusion that the power of propagation by the microorganism is still preserved. This point of view explains sufficiently the usual symmetrical distribution of the early symptoms, and the mostly asymmetrical late symptoms of syphilis.

It is probable that the virus retained in the lymphatic glands and in other tissues may remain inactive for a considerable time, and then be gradually destroyed; but if it reaches the circulation through the vasa deferentia, which it may do after years, then relapses occur in remote tissues. These recurrent lesions may, according to the amount of virus, be plentiful and symmetrical, or appear only in one part. The activity of the virus may also be revived in the lymphatic glands themselves, and so occasionally produce late symptoms.

The connection between the contagium thus conceived and the pathological symptoms of syphilis, therefore, is as follows:

In the beginning the generalization of the contagium produces the irritative conditions, which show themselves in hyperæmia, slight inflammation, infiltration, and hyperplasia. Usually these lesions recede, but occasionally they are not absorbed and may then form more or less permanent nodules in the skin and mucous membranes (tophi).

The gumma requires for its development a residuum of the syphilitic virus in the tissue, probably very much changed, and which may,

excited by some cause to renewed activity, produce certain gummatous lesions. And although it is probable that their origin is usually a germ which may have remained for a long time inactive on the site of the future gumma, it is also possible that such a remnant of contagium may be carried to some other place and produce the gumma there. But while the irritative processes only very rarely lead to permanent new growths of connective tissue, yet connective-tissue products become often very prominent in the parts about the gumma, and the more so the more this is diffused (hepatic, testicular, and muscular indurations, osseous sclerosis, etc.). We may easily imagine that the contagium can even become extinct in places where there remain permanent formations of connective tissue induced by irritative or gummatous processes.

This appearance of gumma infiltrations before the irritative symptoms have completely run their course is to be explained, on the basis of our conception of the contagium, by the fact that it undergoes certain changes in some parts earlier than in others; and that in such cases the virus, stimulated by external influences, has progressed so far that it may produce a gumma, while in other places it causes irritative conditions.

These conditions may explain another fact. It has been asserted that the contagium of syphilis retains its faculty of reproduction in healthy persons only for a certain time, probably coinciding with the time during which it may produce symptoms of irritation in the syphilitic subject. Since we find gummatous products in certain parts, while in others there are yet symptoms of irritation, we must explain the possible existence of infection by the assumption that it remains only in that part of the virus which has not yet lost its irritative property. But as conditions of irritation in organs which are not accessible to careful observation may escape discovery, it is not certain that the infectiousness existing at a time when apparently only gummatous symptoms exist, is associated with those lesions.

As we assume that the essence of the syphilitic virus consists in a microorganism, so we have to consider a series of symptoms to which the host (the infected person) is exposed by the products of metabolism of these microorganisms. Although we shall not be able to judge of these conditions accurately until we have learned more of this microorganism, and especially of its biological character, it is plain that we may reason by analogy from other well-known infectious diseases and may apply the conclusions thus arrived at to syphilis. It has been demonstrated in the case of various pathogenic microbes that they furnish certain active products of metabolism (toxins), which are by no means indifferent in their action, and it is

more than probable that various disorders of the system are based not so much on the multiplication of the parasites as on the poisonous effect of their products (toxins). The malaise usually accompanying the generalization of syphilis, the general depression, the fever (as I noted as early as 1884 in the first edition of my lectures on syphilis), certain alterations in the nervous system, and various other disturbances may well be the result of such a product of metabolism of the syphilitic microorganism. It is more than probable that grave and permanent disorders of the nervous system or elsewhere may arise therefrom.

Besides this noxious influence of the supposed product of the specific microorganism, we may also ascribe to it a beneficial effect, because it is probable that the tissues thus impregnated with it undergo such a change that new infection becomes thereby impossible (the "tissue immunity" of Behring).

Following this presentation of the subject, we may divide the changes occurring in the course of syphilis into two groups: The first includes those pathological products which are to be considered as a direct result of a formative irritation caused by the virus deposited and increasing in the part; such are the initial lesion, lymphangitis, and lymphadenitis, and also the intermediary forms of the disease and gummatous deposits of various kind. The frequently observed serpiginous advance (circular and semicircular forms) of the gummy infiltrate speaks in favor of it being a vital expression of multiplying microorganisms.

The second group includes those symptoms which are produced by the action of the products of metabolism of the syphilitic contagium —symptoms which are comparable to the effects of poisons. This includes syphilitic fever, affections of the nervous system (palpitation of the heart, neuralgia, etc.), and certain forms of anæmia; it is also probable that these toxic products may occasionally cause degeneration (of blood, nerves, etc.). As we said before, these products may also create immunity to a new infection.

But this brief sketch based upon the microparasitic theory of syphilis will be modified in various ways by the presence of other pathogenic microorganisms; we shall examine these modifications more closely below.

The infectiousness of the syphilitic contagium is by no means absolute, and it has often been observed that if two persons are exposed in the same way, one of them may escape infection, apparently being without the necessary predisposition. While this may be due in part to the fact that a port of entry of the virus in that person is missing (no cracks, abrasions, or the like), it is not always so,

for inoculation experiments also show that some persons are immune. Perhaps this may be due to a temporary indisposition for infection, as we see occasionally in the case of dermatomycoses.

It is furthermore certain that the contagium itself, even during the time of its infectiousness, may act variously as regards the intensity of its effects. In hereditary syphilis we observe that the children who are born later are less intensely affected; but it is doubtful whether the same change of effect is produced in extrauterine contagion, and whether this weaker infectiousness is in relation to the duration of the disease. The difference, however, is usually found in the conditions of the person exposed to infection.

Persons who have once had constitutional syphilis are rarely susceptible to a new infection, and some authorities claim even absolute immunity for them.

This belief in the impossibility of reinfection, which was strongly asserted by Ricord, was prevalent for a long period, until observers like Zeissl and Vidal de Cassis disproved the law and were supported in their assertions by later observations of others. I myself have had occasion to observe almost every year cases of reinfection, and the possibility of it can no longer be doubted. But that the previous disease has left its impress is shown by the fact that in the great majority of these reinfected cases the disease pursues a very mild course; in a large number there are no constitutional symptoms whatever, the infection is limited to the initial lesion (which, however, is apt to be very pronounced), and even the indolent buboes are missing oftener than in other cases. As according to our present views only a person perfectly cured of syphilis can be reinfected, we may draw certain conclusions from these observations as to the length of time necessary for a cure. The longest period between the first and second infection is given by Köbner as twenty-one years, the shortest as fourteen months; the most frequent intervals he found to be between six and two and one-half years; the final symptoms after the first infection had disappeared for from twenty years to eight months before reinfection occurred, but old products of the first infection, such as sarcocele or exostoses, might still be present as residue at the time of reinfection. I myself have observed reinfection repeatedly, and I possess careful notes of seven cases. In two of these reinfection occurred about five and one-half and twelve months after the first infection (two and one-half and ten months after the cessation of general treatment); in the other cases it was two, four, five and one-half, six, and eight years after infection, and one and three-quarters, three and one-half, four and one-half, five, and one and one-half years after the last general treatment.

Most cases had been treated with mercury, which is significant as showing the efficacy of this mode of treatment.

Gascoyne and J. Hutchinson have even observed instances of third infection.

In 1885 I saw for the first time reinfection in a person who had recovered from hereditary syphilis.

A waiter, 25 years old, whose father had in his youth recovered from syphilis, and whose mother had died from tuberculosis, said he was the youngest of several children, all the rest of whom died soon after birth. He himself was in good health up to his sixteenth year. He then suffered from ulcers on the right leg, which were treated and cured by a Vienna physician by means of inunctions (forty in number), iodoform, and iodide of potassium. Two years later ulcers in the throat appeared, which destroyed the uvula. He was then treated by iodide of potassium, gargles, and painting with iodine. In 1885, after a coitus, he observed ulcers on the penis. When I saw him, October 24th, 1885, the uvula was missing and a part of the right arch of the palate; the left arch and the velum were seamed by scars; on the right leg there were numerous scars with sharp borders, whitish and shining, with a pigmented border; the tibia was thickened, but not sensitive. On the inside surface of the prepuce on both sides of the frænum I noted a characteristic syphilitic initial sclerosis, partially ulcerated; the lymphatic glands of the right side were enlarged. On November 11th, after the application of emplastrum hydrargyri, the indurated ulcer appeared to be thinly covered by fresh epithelium; but after this I lost sight of the patient.

Since that time I have repeatedly seen fresh syphilis papulosa in several persons (women of the street, young rowdies), who had undeniable symptoms of former hereditary lues (nasal depression, great defects in the septum, characteristic scars on the body, etc.).

As in the large majority of cases syphilis is acquired during a coitus with a syphilitic person, the seat of the initial manifestation is usually the genitals and their vicinity—genital and paragenital initial lesions. So far as we know, parts covered with intact epithelium are not easily infected, and the principal points of contagion are therefore those parts of and near the genitals which are easily torn or abraded. In man the principal place is, therefore, the inner surface of the prepuce, and especially the frænum, which is so prone to be torn, or the free border of a narrow prepuce. Often it is the tender skin of the glans and of the sulcus behind the corona, which is macerated by a thick deposit of smegma. Cases of initial infection on the other parts of the penis or the scrotum or inside the urethra are less common.

In women the most frequent seat is one or both nymphæ or one or both of the labia majora, the prepuce of the clitoris, or the remnants

of the hymen at the introitus; a less common localization is the wall of the vagina, but an initial lesion of the portio vaginalis is not extremely infrequent. Infection on the perineum, groin, or mons Veneris is not infrequent in women, sometimes also in men.

If human aberration leads to unnatural contact of the genitals with other parts, as in the cunnilingus (qui opus peragit linguam arrigendo in cunnum—φωνικίζειν), the fellator (si quis vel labris vel lingua perfricandi atque exsugendi officinus peni præstat—λεσβιάζειν), the irrumare (penem in os arrigere), or any other "coitus illegitimus," then we may see the initial lesion on the tongue or the vermilion border of the lips, in some part of the mouth or pharynx, or in other parts which may have been exposed to contact with the specific virus. This is the extragenital initial manifestation.

By the same law we find initial manifestations on the lips of adults and children who have been kissed by syphilitic persons, or of infants who have been nursed by syphilitic persons; and also on the breasts of nurses who have suckled syphilitic children. Physicians, midwives, nurses, or others may be infected through an abrasion or wound of a finger (and especially in the nail groove), during the examination or treatment of a syphilitic patient. Sometimes the initial lesion may appear where a bite has been inflicted by a syphilitic person. Infection of syphilis has also been produced by tooth transplantation. Once syphilis was caused by a Reverdin skin graft, taken from a person who was afterwards discovered to be syphilitic.

Curious customs prevalent in certain localities produce peculiar local manifestations. So we find in Russia primary lesions in the eyes of children, resulting from the custom peculiar to peasants of that country of licking the eyes of children suffering from ophthalmia. Another example is the infection of the penis after ritual circumcision, if the operator who sucks the fresh sore has syphilitic lesions in the mouth. We shall refer to cases of this sort more in detail in a later section.

In all the cases above mentioned, the infection is produced by direct, more or less intimate contact with the infected person; or the infection is the result of direct implantation of the syphilitic virus. And in these cases it is generally supposed that the infected person had an abrasion, or a fresh or old crack, or else a wound or an open (suppurating) sore at the point of infection, which was besmeared with the purulent secretion or the blood of the infecting person; and also that the virus was yet in the state of irritative contagiousness. But the further possibility exists that very tender epithelial layers or openings of follicles, which may have been in long contact with the syphilitic pus or blood, may be infected without previous lesion. But it may be that in such cases the long contact may have first pro-

duced a maceration of the thin epithelium before the virus penetrated the part.

Very important clinically are those modes of infection which do not depend upon direct contact with a syphilitic person, but upon indirect contagion. To these belong infection from eating and drinking utensils which have been used by a syphilitic person, and have not been thoroughly cleaned; needles used for tattooing; soldering irons, wind instruments, glass-blowers' tubes (syphilis verrière of Rollet), etc. Other carriers of infection are pipes, cigar-holders, tooth-brushes, handkerchiefs, towels, etc.; even cigars manufactured by persons having mucous patches, who lick the end of the wrapper, may carry syphilis.

Some years ago I observed an initial lesion on the forehead after the opening of a boil, which was undoubtedly due to the knife not having been clean. But infection with medical instruments is not likely to occur, now that antiseptic methods are so universally employed.

In many cases the method of infection is almost or quite impossible to detect. Remarkable cases of indirect infection are those in which the disease is contracted through contact with a person who has been in contact with a syphilitic without himself having been infected. Such observations have been repeatedly made by the older authors. The following case, reported by Bertin, is a practical example of such infection by means of a third healthy person.

A perfectly healthy woman nursed her healthy baby for three months. By chance a strange baby was given her to nurse, which baby had syphilitic lesions on its lips. By the end of a week the first baby had a chancre on its lips and buboes on both sides of the neck, which were followed a few months later by a pustular syphilide. But the breast of the mother, by whom the baby was undoubtedly infected, did not show the slightest erosions or ulcerations. The mother retained her health all the time.

The chief and most dangerous vehicle of the syphilitic contagium is, according to the teachings of experimental and clinical experience, the secretion of the syphilitic initial lesion, and that of moist papulæ, mucous patches, cracks and chaps, or erosions, and also the ulcerating or broken-down products of constitutional syphilis possessing inflammatory and irritative or simple hyperplastic character.

The blood in constitutional syphilis has also been found to be a very effective agent of infection, but it does not seem to possess the faculty of transmitting the disease to others in the same degree, for experimental blood inoculations have often been negative in their results. The cause of this failure may be that the contagious prin-

ciple does not remain circulating in the blood for a long period, and that the infectiousness of this physiological fluid is reawakened only after the introduction of new germs from some disease centre in which the contagium has propagated. This observation, in connection with other clinical experiences, warrants the supposition that the syphilitic virus consists of a microorganism which exists and reproduces itself usually in the tissues, and which only occasionally reaches the blood; belonging, therefore, as Baumgarten says, to the class of tissue parasites, not to that of blood parasites.

The spermatozoa and the ova are very important carriers of the contagium of syphilis, as the transmission of the disease to children by the father as well as by the mother shows. That a syphilitic man may infect a woman by the semen alone is probable, but hard to prove.

Although we are as yet ignorant as to the fate of the virus in the human body, it is very possible that it may be eliminated in one or another physiological secretion, perhaps while still in an infectious condition. Most physiological secretions and excretions (saliva, milk, urine, etc.) do not contain the contagium, unless they are mixed with pus or blood; and indeed even a purulent secretion, if produced by a complicated process not connected with syphilis, does not necessarily carry the virus with it. That syphilis may be contracted from a cadaver is a fact which I have demonstrated beyond doubt in the case of a professional colleague.

INITIAL LESIONS.

If a person not previously syphilitic, or one who has been cured of it, is infected by syphilis, the point of entrance of the virus, if it happen to be an abrasion, a cut, a puncture, or any trivial injury of the skin or mucous membrane, in the absence of other pathogenic microbes or injuries, will heal in a few hours like any other slight lesion. Nor does the point of entry within the following few days (*period of incubation*) present any evidences of a special infection or injury.

But after the period of incubation, if the poison has taken effect, an initial manifestation appears in the form of an infiltration, which from the beginning is marked by slight redness, sharply defined borders, induration, and slight sensitiveness; these characters, especially the hard, sharp borders, persist for some time; this first product is called syphilitic chancre, syphilitic induration, or simply chancre or induration (Hunter's induration, or Hunterian chancre).

At other times the infiltration has the form of a sharply defined, not very hard nodule, projecting above the level of the skin, which is called the initial papule or syphilitic papule.

The Chancre.

Histological examination of the chancre shows a proliferation of the cells of the cuticular connective tissue, which in the beginning are found along the smallest blood-vessels, and the process must therefore be regarded as in part a proliferation of the elements of the walls of the vessels, and in part also a migration of white blood corpuscles. In the course of its further development the new formation of cells extends between the small blood-vessels, so that finally the papillary layer, the rest of the cutis, and the subcutaneous tissue appear equally infiltrated. Gradually we observe in the vessels thickening of the media and proliferation of the intima—changes which are found in arteries as well as in veins, and which finally produce contraction and even obliteration of their lumen. These processes remind us of endarteritis and of endophlebitis. The same changes are not seen in the lymphatic vessels, the lumen of which may even appear enlarged.

Corresponding to the sclerosed part we find sometimes interpapillary epithelial depressions of various shapes, like pegs or offshoots, penetrating through the infiltrated cutis; at other times the borders between the papillary layer and stratum Malpighii are obliterated. In such cases the new cells of the cutis are forced always towards the surface, the epithelial stratum appears thinner and thinner, and finally disappears (erosion), or the infiltrated cutis, deprived of its epithelium, breaks down entirely (ulceration). In retrograding chancres we find few cellular elements, but shrunken threads of connective tissue. In old chancres giant cells are occasionally found, as also other changes similar to those existing usually in a gumma. The formation of new cells occurs also in the papillary layer, sometimes extending into the subcutaneous stratum, but principally confined to the papillary layer, starting from the blood-vessels; the papillæ are usually longer and broader, and the interpapillary ingrowth of epithelium is often interspersed with proliferating young cells. This causes a moistening of the epidermis, and soon leads to desquamation.

Symptoms and Course.

The syphilitic chancre occurs as an infiltrate, from the size of a lentil or pea to that of a shilling, which lies in the skin or mucous membrane and the underlying connective tissue as a sharply delimited body, projecting somewhat above the surrounding level and appearing reddish in color.

The form of the infiltrate varies according to the anatomical struc-

ture of its seat; if it is on thin skin with a loose subcutaneous cellular tissue, it has a flat or plate-like extension, in which form it is easily recognized; it is sufficient to grasp the edges between index and thumb to feel a cartilaginous or hard plaque (parchment induration). The comparison to a flat plate of cartilage appears the more fitting if the chancre occupies the inner surface of the prepuce; if we try to turn the inner lamella outwards, the part of the prepuce which the chancre occupies appears like a stiff plate and is bloodless, just like the conjunctiva when turned under the tarsus. The more experienced observer will thereby easily recognize an indurated chancre, and the diagnosis will be confirmed by subsequent examination. If the sclerosis occupies the free border of the prepuce or the urethra, it will give the impression of a stiff tube.

Although usually the superficial extension of the sclerotic infiltration is pronounced, it may have a circular, semicircular, cylindrical, or bean shape; but when grasped between the thumb and forefinger it can generally be felt to be doughy, indurated, and with more or less sharply defined edges.

These forms are, as we said above, usually more pronounced when they are located in loose tissue than when the skin is thicker or when the sclerosis lies over unyielding subcutaneous tissue; in women this difference becomes more conspicuous, if scleroses on the labia minora or on the prepuce of the clitoris are compared with scleroses on the labia majora or on the rough skin of the thigh.

The diagnosis is even more difficult if the indurated chancre is in the cavernous tissue of the glans or in the muscular stratum of the cervix; in the latter case an indurated cicatrix, the remains of a laceration occurring during childbirth, may be mistaken for a syphilitic sclerosis. After having learned to recognize chancres in the usual places, it will not be difficult to recognize them also in less accessible places, such as the vagina, or in extragenital situations, as on the lips, nipples, etc.

We note as a general rule that the infiltrate, which underlies the chancre, increases in proportion as the patient is neglectful of it. When it is carefully attended to, the infiltrate will gradually diminish in the course of a few weeks; it shrinks into a simple thickening of connective tissue, which sometimes remains for years. I could recognize in a man of seventy years, with gummy ostitis on the hard palate, the remains of an indurated chancre acquired when he was very young. Sometimes, however, the retrogression is so rapid and so complete that no trace of induration can be found after a few weeks; and occasionally the originally indurated part becomes atrophic, cicatricial, thin, and poor in pigment. All this may occur, espe-

cially when the lesion is of limited extent or in some inaccessible place, without any appreciable injury to the patient, so that he may deny in good faith any knowledge of an initial lesion; and he may even shake his head incredulously when the physician shows him an old connective-tissue induration or a colorless, atrophied cicatrix on the penis. Sometimes even physicians may overlook the infiltration, as it is so trivial that it can hardly be seen or felt. Even physicians of experience may in such cases reserve the diagnosis of syphilitic infection, because of the limited redness and the very slight induration.

If the initial lesion is inside the preputial sac, the epithelium soon desquamates, leaving a limited erosion, discharging some secretion, and the chancre then resembles a posthitis or balanitis.

Ordinarily the epithelium covering the chancre desquamates early, leaving the corium as a light red, shining surface, often covered with thin, sticky pus; this is the erosive or desquamative chancre. In dry places this secretion becomes a thin, stiff crust. In other cases the secretion destroys the corium also, and a loss of substance results, leaving an ulcer; this is now called exulcerative sclerosis, ulcerative chancre, hard or indurated chancre, the Hunterian chancre, infectious chancre, etc.

A chancre so often and so early, probably because of the access of pyogenic cocci, assumes an ulcerated form, that some clinicians erroneously reverse its stages and assume that the ulcer comes first and then the induration; this is absolutely incorrect, for such cases at least in which there is pure syphilitic infection without complications.

In ulcerated scleroses we find additional symptoms, produced by the destruction of tissue and the formation of the ulcer. The loss of substance rarely involves the whole extent of the sclerosis, but usually only the middle portion and without extending through the entire thickness. As a consequence of this, the principal characteristic of the chancre becomes the fact that it is situated on an indurated base and is either partially or entirely surrounded by a hard, sharply defined border. For the same reason the edges of the ulcer are usually adherent, not undermined; the ulcer is generally shallow, but is sometimes deeper in the centre. The base of the ulcer is more or less discolored by adherent sloughs, but is sometimes of a fine red color and granulating. The pus is shiny, and often contains shreds of broken-down tissue; its quantity is proportionate to the size of the ulcer.

The destruction of the ulcerated chancre may prevail to such an extent that at first sight it has all the appearance of a simple ulcer, but more careful examination soon shows that the margin and bottom

of the ulcer have the clear characteristics of a sharply limited induration. When even the greater part of the lesion ulcerates, there always remains an excavated, dish-shaped part, the outer surface of which forms the seat of the concave ulcer.

Ulceration of a chancre is caused by various conditions. Its histological structure, which shows endarteritis and endophlebitis, explains how the disease of the vessels may lead to gangrene. Thus we observe occasionally bloody, necrotic shreds of tissue in the centre of the open chancre, and the gangrenous process may even extend sometimes over the whole surface of the initial lesion, and in that case the superficial layer of the chancre appears as a blood-soaked eschar; this is the gangrenous chancre.

Again, we must not forget that various pathogenic germs may lodge on an open (ulcerated or gangrenous) chancre, which may alter the clinical picture. These are, besides the contagium of the venereal ulcer (soft chancre), the pyogenic cocci, especially when cleanliness is lacking. The destruction of tissue is rapidly increased by the inflammation produced by these microorganisms. The more the lesion extends towards the surface, and the greater the maceration which the epithelial layer undergoes, and also the more the person is careless and uncleanly in his habits, the sooner will erosion and ulceration take place. Ulceration is favored also by the movements of the parts and the consequent stretching and pulling in different directions of the infiltrated lesion.

We have repeatedly shown that the syphilitic virus usually gains entrance in parts which are naturally disposed to erosions, tears, etc.; but the tendency to such lesions is increased by the pathological changes emanating from the initial manifestation, as these cause a loss of the normal elasticity of the tissue.

The further course of the ulcerated chancre is unfavorable, if by carelessness or improper treatment inflammation is excited; then we observe redness and swelling of the neighboring parts in addition to the initial lesion, and other complications, such as erysipelas, gangrene, etc., are apt to arise. These complications may, of course, alter the original appearance of the chancre almost completely.

Sometimes an ulcerated chancre acquires a singular appearance, in consequence of exuberant granulation filling the ulcer and even rising above the surrounding level (ulcus elevatum). In rarer cases the chancre becomes the seat of papillary excrescences, which may assume the appearance of warts, arising from a base from the size of a hempseed to that of a pea, or which are attached by a slender pedicle and form a growth with several lobes of various forms and sizes. These formations—which are usually called pointed condylomata—

are called by me venereal warts, papillomata venerea. These sometimes develop alongside of the other syphilitic forms.

The ulcerated chancre improves almost without exception under appropriate treatment. The ulcer begins to clean, and a fresh growth of the epithelium begins to form at the periphery after a few days; the secretion of pus diminishes, and in a short time the loss of substance is covered by new skin. But this is not the end. The careful observer will see that the sclerosed part on which ulceration had existed has meanwhile decreased a little in area, but that further diminution proceeds very slowly, just as in the non-ulcerated sclerosis. It is in such cases often difficult to make the patients understand that the course of the initial lesion is not finished with the cicatrization of the ulcer, and that there is danger of fresh eruptions while induration persists. Nor must the physician forget this, else he will not understand why and how sooner or later new ulcers arise in the same place. It is a fact that a chancre often breaks open again in one or the other part after such cicatrization, or that the initial lesion is but superficially cicatrized on one side, while at the opposite border the ulceration deepens and progresses. We see this especially in cases in which the initial manifestation changes directly into a lymphatic sclerosis or into an indurated lymphangitis. If in such cases the breaking down of the initial lesion extends to the lymphatic vessels which are affected at the same time, the ulcerative process is often greatly protracted. A chancre in the sulcus behind the corona has a special tendency to extend in this way, and we see the ulceration proceeding along the affected lymphatic vessels, or advancing between the glans and corpus cavernosum, forming by its destruction pockets and excavated ulcers of very chronic course.

It must be mentioned, however, that the chancre sometimes shows only an imperfect tendency to heal, even when there is no affection of the lymph vessels, and leads to progressive ulceration in other parts. In such cases my opinion is that the initial production has undergone a change into a gumma; this change sometimes results in the taking on by the ulceration of a serpiginous character, just as we see in a gumma which is breaking down.

Diagnosis.

In the great majority of cases a chancre is easily recognized, but under certain conditions other changes may occur which give a marked resemblance to the initial lesion of syphilis; such, for example, are scars produced by cauterization with caustic potash or caustic lead. The latter, occasionally used with good results in venereal warts, often leaves cicatrices which may easily be taken for a

chancre or at least the remains of one. At other times a trivial mechanical lesion (desquamation, tear, or fissure) around the genitals may, as we can readily understand, upon the occurrence of a slight inflammation produced by the settlement of pathogenic cocci, assume a suspicious appearance (chiefly because of its situation) without having any connection with syphilis.

We ought, therefore, always to inquire carefully into the history of the case and the chronological order of the appearance of the lesions, and especially also to ascertain the condition of the neighboring lymphatic glands.

A gumma may also (as we shall explain later) be mistaken for an initial lesion.

Certain difficulties may arise if the seat of the original lesion is concealed, as, for example, when a chancre exists within the preputial sac.

When there is phimosis from the beginning, or when the initial lesion within the prepuce is accompanied by a contraction of the ostium cutaneum, a so-called inflammatory phimosis, it is impossible to see the lesion in the sac of the prepuce; but even then we are usually able to diagnose a chancre. Externally there is no change visible; or there may be, at the site of the chancre, a small protuberance of a more or less red color. But if we palpate successively the glans, corona, sulcus, and frænulum, we shall be able to detect the existence of an induration. The firm, uneven surface of the sharply defined, indurated, and sometimes sensitive infiltration is so marked that it can hardly be overlooked. The occurrence of a discharge from the preputial sac is dependent upon the degree of erosion or ulceration, and is of no diagnostic value.

If the external surface of the phimotic prepuce is intensely red and swollen, and especially if it should be very sensitive in one or another part, but without the above-mentioned symptoms characteristic of chancre, we may suspect the existence of a soft chancre in the preputial sac. If these symptoms are absent, an existing discharge from the preputial sac may be regarded as due to gonorrhœa or to a simple or herpetic balanoposthitis. Initial lesions on the mucous membranes present usually the same clinical aspects as those on the skin; but the epithelial layer desquamates sooner in such cases, and consequently erosion and ulceration are more common results. The induration is then ordinarily covered with a whitish, scurfy epithelium, or is converted into an ulcer, more or less coated with secretion, or occasionally red and smooth. What we have said above applies equally to the diagnosis of this lesion.

Urethral chancre deserves especial mention on account of its con-

cealed situation. We may find it in any portion of the urethra, from the meatus to a point 2 or 3 cm. (about one inch) above the fossa navicularis; above this it hardly ever develops. Erosion usually follows quickly and produces some mucopurulent or frankly purulent discharge, which draws the attention of the patient to the possibility of a gonorrhœal infection, although he cannot understand why it appears so long after the coitus. The burning sensation which accompanies gonorrhœa during micturition is absent or very mild, but the fact of a discharge from the urethra induces the patient to seek advice of a physician, who on superficial examination readily enough diagnoses a mild urethritis. Careful examination of the anterior portion of the urethra soon shows a circumscribed, hard, sometimes sensitive infiltration of cylindrical or spindle-like form, 1 or 2 cm. in length. Its longitudinal axis coincides with that of the urethra. The infiltration can be easily found by pressing with the thumb and index finger the glans, sulcus, and other parts of the penis one after the other in regular order, and by palpating the urethra laterally. We ascertain in this way that the sclerosis occupies either the whole circumference of the urethra or simply one part of it. Rarely we find two or three perfectly distinct tumors. Sometimes there is at the same time another initial lesion externally on the penis or some other part. On endoscopic examination the introduction of the tube reveals a stricture of variable calibre, according to the degree of infiltration; we must therefore use a smaller and shorter (5 cm.) endoscope. With this we are able to detect a displacement or a distortion of the central image, according as the sclerosis is cylindrical or occupies only one side of the urethra. If the eroded or ulcerated surface of the chancre is coated, we see a difference in color after removing the thin layer of secretion.

We would note especially the fact that in gonorrhœa considerable swelling and infiltration of the urethra occur, and this may very closely resemble a chancre of the part. Ordinarily this inflammatory infiltration of the submucous layer, when it is very extensive, occupies a large part of the urethra; but even when it is only in a limited portion, the copious secretion and the existence of gonococci will prevent confusion.

Venereal ulcers also appear in the anterior portion of the urethra; they may be suspected when we find considerable sensitiveness, swelling, and redness, but no sharply circumscribed induration in the urethra. The endoscope makes the recognition sure.

The Initial Papule.

The initial lesion appears somewhat less frequently in the form of the papule than in that of the indurated infiltration. After the period of incubation a small, sharply defined nodule, the size of a lentil or a pea, or even larger, of a dark blue or pale red color, is seen at the point of entrance of the virus. The infiltration does not extend, as in ordinary chancre, to the subcutaneous or submucous tissue, but superficially. The initial papule, if left to itself, often reaches the size of a silver ten-cent piece, or even larger. The smaller ones are hemispherical in shape; the larger ones are less elevated, although still projecting a few lines above the level of the surrounding integument, and present a flat surface. Such a lesion is known as the flat or broad syphilitic papule.

The appearance differs according to location. When seated on a dry part of the general surface, the primary syphilitic papule appears as a low-arched or a flat, sharply circumscribed, dirty or bluish-red, livid nodule. At first it is hard to the touch, but not so hard as the initial sclerosis. But gradually the infiltration becomes softer, and this is the more pronounced the greater is the elevation of the papule above the surrounding integument. The epithelial layer is thickened, and in the centre there is a branny desquamation, while at the periphery the loosened edge of epithelium remains adherent for a long time. Usually the epithelium which covers the infiltration is not sufficient to protect it against the surrounding moisture; hence some fluid penetrates from without and agglutinates the loose epithelial scales; these, becoming dry, form a more or less thick crust.

If, however, the papule is located on a part of the skin which is moistened by physiological or pathological secretions, the epithelium covering the initial lesion becomes immediately macerated and forms, with the moisture of the papule and the other secretions, a pultaceous, pus-like mass, adherent to the surface—the moist papule. This adherent greasy mass, usually the home of all kind of microbes, is considerably increased in amount by the secretion of the neighboring glands, and decomposes into a stinking mass. When cleaned of this layer, the papule appears like a succulent nodule of the skin, with a broad base, the surface of which is whitish and covered with adherent, scurfy epithelium; or if this has desquamated, the lesion is red; or, finally, the surface presents alternating red and white miliary granulations.

On mucous membranes the papule presents a different appearance. The nodule hardly extends above the surrounding level, and the epi-

thelium changes early into a whitish scab, partially adherent for a time and then separating, leaving a swollen, red, slightly bleeding surface.

When located on a mucocutaneous surface, partly on the skin and partly on mucous membrane, the lesion has a characteristic appearance. It combines then the characters of a cutaneous and a mucous papule.

Wherever it may be situated, however, it breaks down in the same way as the indurated chancre, and forms an ulcerated papule. But we find that the ulceration in such cases involves the entire papule and the whole lesion becomes destroyed, so that there results a sharply circumscribed, dirty ulcer, extending more or less deeply, the edges and base of which show traces of the infiltration, together with an inflammatory swelling; but it is scarcely possible to recognize here the initial papule.

The papule breaks down the more readily the more it is irritated by uncleanliness or unsuitable local treatment, or is exposed to mechanical insults. A papule located at the preputial orifice, or on other parts exposed to stretching, quickly ulcerates or shows tears or cracks. These are often very painful.

Venereal warts, papillomata venerea, have been observed on ulcerated papules, but this is rare. The initial papule has the same tendency as the initial sclerosis to heal promptly if properly treated. As long as it is not ulcerated, it diminishes steadily by absorption of the infiltration, especially at first. The initial redness, which is sometimes dull and sometimes bright, diminishes in intensity and is succeeded by a dirty-brown or gray pigmentation, corresponding in extent to the original size of the papule. Traces of the papule persist sometimes for weeks, but often it disappears entirely, as does also the pigmentation, which may be replaced by a white spot, that betrays the original lesion even years after. In some cases this retrogression is incomplete and the evidences of the papule remain permanently; we have a solid, pale brownish papule, sometimes of the same color as the skin, and in its epithelial covering also may differ in no way from the surrounding parts. I have seen such normally colored papules behind the sulcus glandis or on the labia majora, at the site of the original infection, after the lapse of years. In the case of a moist papule, or a suppurating one, deprived of its epithelium or partly broken down, furrowed by cracks, or with its entire surface occupied by an ulcer, we occasionally see an acute inflammation or some other complication, such as erysipelas, diphtheria, or gangrene. As a rule, however, the observance of cleanliness and proper treatment usually bring about drying of the moist

papule, and this is followed by recovery. Even when there are cracks and ulcers, recovery follows proper treatment; the ulcer begins to granulate, the edges become level with the surrounding integument, and the whole has the appearance of an ordinary suppurating surface. Healing occurs with the formation of a sharply circumscribed and usually depressed scar; this is commonly surrounded, when the ulceration involved only a part of the papule, with a pigmented zone, corresponding to the intact portion of the papule, which remains for some time but finally disappears.

When the initial papule is seated on mucous membrane, retrogression begins with decreasing infiltration and disappearance of the bluish-white, scurfy epithelium; then a red surface remains, covered occasionally by a delicate whitish veil. The spot gradually decreases in area, having at the periphery a fresh, concentrically advancing border of epithelium, and in the course of a few days is wholly covered with new integument; this latter usually persists as long as the infiltration continues to recede. Usually nothing at all remains to mark the site of the original lesion; even when the lesion has been marked by cracks and ulcers, it can usually be recognized only by a scar, which seems whitish by comparison with the surrounding mucous membrane. While, therefore, a papule on the general skin can be recognized for years by a disappearance of pigment or a cicatrix, a papule on mucous membrane leaves no permanent traces after its disappearance.

Seat of the Initial Lesion.

The syphilitic initial symptom, whether it be erosion, sclerosis, or papule, is very often, perhaps usually, single; yet it is not rare to observe two, three, or more lesions on as many different places—as, for example, the prepuce, glans, and urethra, or the clitoris, remains of the hymen, and labium majus. It can be easily understood that if, at the time of exposure, the necessary conditions for infection exist in several places, the initial lesions may be multiple; sometimes the lesions are both genital and paragenital, and occasionally they may exist on widely separated parts. Jonathan Hutchinson, A. H. Ohmann-Dumesnil, and myself have observed such cases.

The seat of the extragenital infection varies a great deal, and no part of the body is spared if the conditions for infection are favorable. In case of infection through kissing, which is of frequent occurrence, the initial lesion is ordinarily found on the lips, corners of the mouth, tongue, or face; but occasionally also on other parts, as the eyelids or conjunctiva, the ear, or even the toes (Leloir).

Undoubtedly infection may also be produced by various utensils

and household articles. The seat of lesions so acquired is usually the mouth, but they may be found also in various other parts. I have seen marked initial lesions on the fingers, in the palm of the hand, on the nipples, forehead, chin, nose, eyelid, gums, tongue, tonsils, hard palate, etc. The tonsils are especially liable to infection, because of their lacunæ.

It can be readily understood that the anatomical and physiological peculiarities of the affected parts, as also the special sorts of injury to which these may be exposed, give rise to certain departures from the normal type. An indurated chancre on the tonsils, for example, ulcerates readily and may be very sensitive during mastication; initial lesions on the tongue are often very troublesome, and the erosion and ulceration which are usually present occasion severe pain in eating, drinking, and speaking; lesions on the lips or at the corners of the mouth become cracked in consequence of the unavoidable movements of the parts.

Initial lesions on the fingers are also more or less painful, according to their seat. In case of a sclerosis or papule near the nail or its root, the infiltration swells outwards like a fungus. The infiltration under the nail produces intense pains, which are increased if the granulations are cut off or incised. A panaritium sub ungue develops, in the course of which the nail is often shed and a new one is formed. A feeling of coldness and other sensations, not always easily described by patients, remain for some time.

Weak Initial Manifestation.

The chancre and the papule are the most trustworthy evidences of the existence of a syphilitic infection. The indurated chancre is of more frequent occurrence than the papule. Up to the present we are unable to say why a chancre appears in one case and the syphilitic papule in another. Although in the large majority of cases (ninety per cent., according to my own experience, less according to that of others) either a chancre or papule is the first symptom, there are also cases in which the initial lesion is very slight or wholly wanting. In such a case the point of entrance of the virus is shown by a simple fissure or a slight erosion of the skin or mucous membrane, or by nothing at all. These are most certainly cases of syphilitic infection without any clearly marked initial manifestation, or rather (more probably) with a very slight development of the local affection.

In women who are infected by means of the semen or during conception, the local lesion may be absent or difficult of proof. And even in those cases in which the initial manifestation of syphilis is present, the intercurrence of other processes acting at the same point may

modify very materially the character of the lesion. We need only remember that the same solution of continuity which has given opportunity for the entrance of the syphilitic virus may also admit other excitors of inflammation, which may interfere with the ordinary development of the symptoms in loco infectionis. In this we find a ready explanation of the engrafting of acute inflammatory changes, in the form of erysipelas, phlegmon, and the like, upon the local luetic manifestation.

Indurated Œdema.

A very peculiar modification of the clinical picture is that in which a hard œdema is added to the initial lesion. As is partly indicated by the name (œdema indurativum, of Sigmund—œdème scléreux, of Fournier), this condition is one of increase of volume of the affected part in consequence of a firm, œdema-like infiltration in the skin and subcutaneous connective tissue. It is worthy of note that this affection is scarcely ever encountered elsewhere than on the genitals.

While this indurated œdema is usually seen in connection with the initial manifestation of syphilis, it may also complicate the lesions of the constitutional disease, usually the papular lesions. Apparently the original syphilitic focus is the starting-point of this affection, which may, however; gradually pass beyond its early limits and reach a greater degree of development.

Thus we find the whole prepuce and also the greater part of the skin of the penis changed into a hard, elastic, even swelling, of such a degree that the member may attain the size of a child's leg. The skin is dark or dirty-brown in color, usually smooth and not pitting on pressure with the finger. The borders of this hard œdema are sometimes indistinct and at other times very sharply limited, and within them the chancre or the syphilitic initial papule is usually plainly to be seen; sometimes we can feel hard, nodular, lymphatic cords through the thick skin of the penis. The affection advances very slowly, and it rarely reaches the mons Veneris or the skin of the scrotum; when the scrotum is invaded, there is an exaggeration of the normal markings of the skin of this region. There is no sensitiveness, redness, or increased temperature—no symptom, indeed, of any inflammatory condition. Mauriac reports one case of this sort in which suppuration occurred.

Left to itself, the œdema changes slowly, but it quickly subsides under local and general mercurial treatment.

In women the indurated œdema develops similarly; the labia majora, the prepuce of the clitoris, and sometimes the labia minora

are affected. If originating from a chancre, the change begins usually asymmetrically, as the initial lesion is usually unilateral. It may begin in one labium majus, for example, and remain on one side for a long time; but at the expiration of several weeks or even months it may extend to the other side, and also up on the pubic region. It is usually found more pronounced in women, as they are more apt to neglect the initial lesion.

Mixed Infection.

The development of the initial lesion of syphilis is profoundly modified when the virus of some other morbid process gains entrance simultaneously with that of syphilis, or when the two contagia are received at two distinct but not widely separated periods.

At the time when humanized lymph was used for vaccination, syphilis was occasionally conveyed by it (vaccination syphilis); but this is not seen now that calf lymph is almost universally employed.

The Venereal Ulcer.

Simultaneous or consecutive infection with syphilis and the contagion of a venereal ulcer (soft chancre) is very interesting and of great practical importance. In order to gain a clearer understanding of it we may profitably outline briefly the symptoms and course of the venereal ulcer or soft chancre.

If the patient himself or another person is inoculated in a part covered with healthy integument with pus taken from a soft chancre which is still in the "destructive stage," there is immediately after the inoculation puncture a slight redness of the skin, lasting for a few minutes only. Then, at the end of from twenty-four to forty-eight hours, there appears at the point of inoculation a small nodule, the size of a millet seed or larger, and surrounded by a red area. Suppuration occurs in this nodule immediately, and within a few hours it is transformed into a pustule the size of a pin's head or larger. The pustule soon breaks or dries up to a scab, which falls off, leaving an ulcer, with a more or less uneven base, encroaching upon the corium somewhat. The border of the ulcer is round or uneven, but always sharply cut. The secretion is thin, cloudy from admixture of particles of necrotic tissue; the adjacent parts are in a state of inflammatory irritation. A similar course is observed when infection occurs during coitus. In the following days we usually observe that the surrounding tissue breaks down, and an increase in area and sometimes also in depth of the ulcer results. The edges and base of the ulcer appear unclean and uneven, on account of the adherent

necrotic particles. In this stage, the "destructive stage," inoculation with a small quantity of the secretion produces an ulcer having the same course and character. But more than this, accidental contact of the secretion with an abraded surface, or even a prolonged contact with a part covered with tender epithelium, results in the production of the same ulcer. This is the explanation of *autoinoculation*, through which several successive venereal ulcers may arise in close proximity to each other in the same person. Sometimes there is inflammatory swelling of the adjacent lymphatic glands, which then usually suppurate (bubo). Sometimes this pus, as well as the secretion of the original ulcer, possesses the quality of producing a new ulcer by inoculation, and in this case the contagium must have reached the lymphatic gland. Sometimes we observe that the virus, in its passage from the ulcer to the lymph glands, excites inflammation in the lymphatic vessels through which it is conveyed, and this lymphangitis results in the formation here and there of small abscesses (bubonuli, Nisbeth's chancre), the pus of which can also cause a venereal ulcer.

The secretion of the venereal ulcer remains contagious, however, as long as the lesion retains its ulcerative character; after the inflammatory reaction has once disappeared and the ulcer has ceased to enlarge by disintegration of the neighboring tissue, when all necrosed particles of tissue which were adherent have been thrown off, we observe that the base of the ulcer clears and normal granulations spring up; the border then appears closely adherent, and very soon encloses a ring of newly-formed epithelium; in a word, we find in place of an ulcer a healthy granulating surface, which is progressing towards a cure. In this stage, which is called the stage of repair, and which generally makes its appearance after the ulcer has existed a few days or a few weeks, the contagium already seems to be destroyed, as inoculations made with the secretion will no longer succeed.

As is the case with the original venereal sore, the second and third which have been produced by autoinoculation, as well as any suppurating lymphatic glands, also lose their contagious qualities in the stage of repair. We will only mention in passing that the venereal ulcer may be attacked by any wound complication, such as erysipelas, diphtheria, or gangrene.

It is only a few years since, while humanized lymph was used in vaccination, that occasionally vaccine virus and syphilis were inoculated simultaneously. In these cases of vaccination syphilis the vaccine pustule and the primary lesion of syphilis were developed independently side by side, in which case their respective incubation

periods were quite frequently sharply defined, perhaps with only slight changes.

A simultaneous infection with syphilis and the venereal ulcer is, from the nature of the case, a not improbable occurrence; or the two viruses may be derived from different sources, and introduced at different times but through the same port of entry. Assuming the case of a contemporaneous action of both contagia, the venereal ulcer with its very short period of incubation will more certainly make its appearance before the syphilitic initial lesion than does the vaccine pustule; it may continue to develop or even progress towards repair and cure during the incubation period of syphilis. The syphilitic initial lesion which develops later will thus complicate the venereal sore in the stage of ulceration or in that of repair, or else will make its appearance after the latter has already healed. In these cases the surroundings and base of the venereal ulcer will gradually assume a sharply defined induration, which, notwithstanding that the ulcer is progressing towards a cure, will develop to a certain degree; or the cicatrix of the ulcer which has already healed will be the locality in which the initial lesion is developed.

If infection with the contagium of the venereal sore has taken place one or two weeks after the syphilitic infection, the development of the syphilitic initial lesion may closely coincide in point of time with that of the venereal ulcer. I have not infrequently seen individuals who had been infected with a venereal ulcer on the same spot where there were still present marked traces of a previously acquired initial sclerosis.

Lymphadenitis.

When a syphilitic initial lesion has made its appearance after the period of incubation is passed, the virus, leaving aside a local spread or postinitial infection, is carried further in the fluids of the body and seemingly most frequently by way of the lymphatic channels. Already in the first or second week after the initial lesion makes its appearance—sometimes nearly contemporaneously, rarely later—we observe that the nearest lymphatic glands become enlarged and present in the early period some tenderness, although no signs whatever of an acute inflammatory reaction are observed in the gland itself or in the skin which covers it. Tenderness also continues only for a few days, so that later on nothing is observed in the neighboring lymphatic glands except their enlargement. From time immemorial lymph-gland enlargements have been called buboes, and these also go by this name, being called *indolent buboes*, to distinguish them from the inflammatory and therefore painful lymphadenitis, which fre-

quently occurs in connection with the venereal ulcer. Rarely one, usually several of the nearest lymphatic glands reach the size of a hazelnut or a walnut, and remain in this condition as a rule for many months, sometimes even for years.

As the initial lesion in the greater number of instances makes its appearance on the genitals or in their neighborhood, the lymphatic glands of the groin are most frequently the seat of indolent buboes. When the primary sore is situated laterally, the lymphatic glands of the same side, when it is in the median line, sometimes the glands on the right, sometimes those on the left, are affected; on account of the manifold anastomoses of the lymphatic vessels in this locality, it does not so very infrequently occur that the indolent bubo may be found on the side opposite the initial lesion, or even on both sides. In a few cases the femoral glands or a small lymphatic gland situated on the mons Veneris also enlarge; at times the chain of indolent buboes extends towards the iliac glands, especially to the first one—namely, Rosenmüller's gland. In isolated cases I have found the glands of the pelvis enlarged to tumors the size of a fist. In exceptional cases we find the inguinal glands only very slightly enlarged, and it is possible that in this case the more deeply situated glands of the pelvis are more involved.

In those rare cases in which the initial lesion makes its appearance in another locality—for example, on the fingers, the nipple, the lips, the tongue, the eyelids, or any other part of the body—the lymph glands in the region of the elbow, the axilla, or the neck, or the preauricular glands become the seat of indolent buboes. We see sometimes that the nearest lymphatic glands (for example, those at the bend of the elbow and the groin) are skipped, and the second in the series (axillary or pelvic glands) become affected.

When patients acquire both a genital and an extragenital initial lesion, simultaneously or nearly so, we find not only the glands of the groin, but also those of the extragenital region enlarged. I have observed this in three cases (in male patients), in which chancres of the chin, of the lower eyelid, and of the finger were present, in addition to a primary lesion on the penis; in each instance the accessory glands of the lower jaw, of the bend of the elbow, and of the preauricular region (besides the lymphatic affection of the groin corresponding to the genital chancre) were characteristically affected. As a rule, the affection of the lymphatic glands following an initial lesion does not go on to suppuration; but as complications, which would in themselves cause a chronic or acute affection of the lymphatic glands, are frequently present, so that other injurious factors besides the syphilitic virus also exert their influence, we find

deviations from the course so far described. Thus suppuration of the lymphatic gland occurs as a rule, if the chancre itself becomes ulcerated, if still another inflammatory process is present at the periphery of the glands (we occasionally find such an inflammation due to the presence of a venereal ulcer), or if the lymphatic gland has itself been affected by some traumatism.

In those cases in which a chronic (scrofulous or tuberculous) swelling of the lymphatic glands was present prior to the syphilitic infection, the characteristics of the lymphatic adenopathy as usually found in connection with an initial lesion will of course be absent; we may then observe, at the most, that an impulse has been given by the newly added factor to a change in the hitherto indolent course of the adenopathy so that, at least in some portion, the infiltration accompanied by œdema is increased and terminates in suppuration. The ordinary indolent bubo is in itself inclined to persist for a long time, but the course of these strumous forms of lymphadenitis, complicated by the occurrence of an initial lesion in its periphery, is an exceedingly slow one. We meet in such cases in one or several places with suppurative adenitis and an œdematous, infiltrated condition of the parts immediately about, the course of which is often very sluggish, so that rupture and exit of the pus come very late. The pus which is evacuated comes from a greatly ramifying sinuous cavity, in which larger or smaller remnants of the parenchyma of the gland are present, which disappear only slowly by suppuration. This condition of the abscess cavity is the reason why, in spite of its contraction, perfect closure takes place only very slowly, and why here and there sinuous fistulæ may still exist after months or, in some cases, even years. In such a case we see in the skin covering the partly shrunken glandular tumor one or more narrow contracted openings from which, as the mouth of the existing fistula, a small quantity of thin puriform fluid can be expressed; occasionally the secretion which has come to the surface dries in the form of a scab, and it is only after the removal of this that one of these sinuses may be seen. From this we see that there are many factors which may lead to suppuration in otherwise indolent buboes.

Lymphangitis.

Somewhat less frequently than in the case of the glands, but still sufficiently often, the lymphatic vessels which lead from the primary lesion to the glands become affected. This complication is most plainly seen in the lymphatic vessels of the penis On the under surface of this organ one or more hard, knotty cords, from the thickness of a thread to that of a piece of string or thicker still, may be

felt under the skin; these are as a rule only slightly tender, and may generally be traced to the root of the penis and from here occasionally as far as the lymph gland; sometimes the affection begins at the seat of the initial lesion, in which case the network of lymphatic vessels situated behind the sulcus may be felt through the skin on one or both sides, as a nodular helix. This *indurated lymphangitis*, as I call it, is not ordinarily accompanied by an acute reaction; we do not, therefore, observe any change in the skin as a rule, though occasionally the latter is œdematous, more rarely reddened in streaks.

The indurated lymphangitis is, of course, met with most frequently on the back of the penis; it may, however, mark the path between the induration and the bubo in other localities as well, as may be seen on the arm and forearm in syphilitic affections of the nail-furrow; in a case of a syphilitic initial lesion of the cheek, I once was able to trace the course of a hard indolent cord from the chancre to an indolent bubo under the lower jaw. I have also frequently been able to demonstrate induration of the lymphatic chains between the labia and the glands of the groin in women. The involution of an indurated lymphangitis is also a question of some time, but the traces of it do not persist so long as those of the initial lesion or the indolent buboes.

Suppuration of any of the indurated lymphatic chains accompanying the initial lesion is rare. On the other hand, an affection of the lymphatic vessels directly accompanying the chancre (especially of the sulcus) may be involved in the breaking down of the latter and cause a creeping ulceration, so to speak, of the diseased lymph vessel.

Differential Diagnosis of the Initial Lesion.

What has already been said is probably sufficient in most cases for the diagnosis of the initial lesion. We should, however, recollect that it may make its appearance in the following forms: (1) Simple (or multiple) chancre; (2) eroded chancre; (3) ulcerating chancre; (4) gangrenous chancre; (5) simple (or multiple) papule; (6) eroded papule; (7) ulcerating papule; (8) slight infiltration; (9) a seemingly simple erosion; (10) fissure.

It must not, however, be forgotten that the list of the varieties of the initial lesion is not exhausted with this; for the chancre may be complicated with non-syphilitic affections, most frequently with the simple venereal ulcer. We may, therefore, imagine that the distinction is occasionally not at all easy between a syphilitic chancre and some other form of disease.

Even the correct diagnosis of a slightly marked initial lesion, and especially the differential diagnosis between a syphilitic initial erosion within the preputial sac and a common *balanoposthitis* may have its difficulties; regarding this condition, the reader is referred to what has been previously said. As regards the chancre situated within the urethra, we also refer to what has preceded.

The condition of the nearest inguinal glands should be investigated under all circumstances; these, no matter in what form the initial lesion occurs, will be affected with the greatest frequency and nearly always at a very early period. We should accustom ourselves, indeed we should make it an invariable rule, not to confine our examination to the suspected initial lesion, but to continue it also to the lymphatic glands in the immediate neighborhood.

As we have already said, the novice is inclined to look upon any inflammation of the genitals, be it ever so benign, as a venereal lesion, especially as a syphilitic manifestation, but an examination into the condition of the neighboring lymphatic glands will quite often save us from making a hasty and perhaps erroneous diagnosis. We should especially remember that the genitals may also be the seat of a simple folliculitis, that herpetic eruptions are quite frequently met with here, and that the itch mite by preference makes its furrows in the skin in this region. It will be sufficient merely to mention these affections.

By the exercise of some care we shall be able to recognize erosions or fissures as such, even when they are in a state of inflammation, and also to distinguish the loss of substance and cicatrices, especially those which have been occasioned by preparations of potassium and which are not very infrequently indurated, from syphilitic initial lesions. The condition of the neighboring lymphatic glands is in many cases directly diagnostic. We must, however, remember that occasionally the glands are only very slightly affected. Finally, we must not overlook the fact that two or more of the affections mentioned above may exist side by side with the initial lesion. By carefully considering the symptoms peculiar to the individual affections we shall be able in the great majority of cases, even under these difficult circumstances, to recognize the nature of the complication present.

The differential diagnosis between the initial lesion and the products of constitutional syphilis, carcinoma, etc., when these make their appearance on the genitals, will be suitably discussed later on.

Just as we are in danger of looking upon genital affections of various kinds as initial lesions, so we may, on the other hand, easily ignore the true nature of the initial lesion when this latter occurs in

some other locality. Whoever has studied closely the clinical character of the syphilitic initial lesion in its various forms, however, will be able to recognize it easily also in its paragenital or extragenital location. After what has already been said, it will be sufficient to add that an initial lesion may make its appearance on any portion of the skin, after inoculation has been successfully carried out, whether in the form of a distinct papule or chancre (perhaps with erosions or ulcerations) or in that of a slight infiltration, or even of a simple fissure, erosion, or desquamation. We need only remember the manifold causes which may lead to extragenital infection and furthermore always bear in mind that the corresponding lymphatic glands are involved as a rule. On account of the great practical importance of differentiating between an ulcerating chancre and a venereal ulcer, it will be useful to present the characteristic symptoms of the two affections in tabular form for ease of comparison. And first, I would expressly protest against the common expression "hard ulcer," "soft ulcer" as being sufficient to differentiate the two forms, aside from the fact that it is altogether wrong to speak of a loss of substance which is either "hard" or "soft."

Syphilitic Initial Lesion (ulcerated).	*Venereal Ulcer.*
The period of incubation of the initial lesion is counted by days, and lasts on an average three weeks.	The period of incubation of the veneral ulcer (if we may indeed speak of such) is counted by hours and last rarely longer than two days.
The initial lesion makes its appearance in the form of an infiltration, which either rises above the surface as a papule or may be recognized in the skin or mucous membrane as a distinct induration.	A small nodule surrounded by an areola makes its appearance at the point of infection, and almost immediately suppurates, that is to say, it is changed into a pustule.
The initial lesion very easily becomes eroded and breaks down, usually forming a shallow ulcer with a reddish lustre, as though varnished, which secretes but little; or else there is a deep ulcer in the centre, which looks as though covered with a deposit of necrosed tissue remnants, having as a rule a closely adherent edge sloping off gradually to the level of the surrounding parts.	After the covering of the pustule is thrown off, or after the crust, which is formed by the drying of the contents of the pustule, is shed, a deep painful ulcer with an unclean base, and sharply cut, irregular and occasionally also undermined edges comes to view.
The base and neighborhood of the ulcer as a rule still present signs of the original initial lesion (induration or papule).	The base and neighborhood of the venereal ulcer for a few days present the signs of an acute inflammatory reaction, which lasts as long as the ulcer is in progress of enlarging.
The secretion of a syphilitic initial lesion only rarely causes symptoms similar to the initial lesion on the patient, the	The secretion coming from a venereal ulcer is capable of giving rise to similar ulcerations in the neighborhood (auto-

Syphilitic Initial Lesion (ulcerated).	*Venereal Ulcer.*
initial lesion is, therefore, very frequently single; the lesions are multiple only when the virus has entered the system at the same time by more than one portal, or in cases of postinitial infection which is of comparatively rare occurrence.	inoculation). For this reason, venereal ulcers are almost always multiple, the lesions appearing successively.
The ulcer (erosion) of the initial lesion very soon cicatrizes when properly treated, although the original infiltration, especially in the case of a chancre, may persist for a long time; as long as this is the case, a return of the ulcerative process is possible.	Healing results only when the ulcer has cleared up and the signs of the acute inflammation have disappeared; when the ulcer is once healed no sign of the former process except the cicatrix will be left, unless an atonic ulcer is present, and thus a recurrence of the ulceration is not to be expected.
Within a few days after the appearance of the initial lesion, the nearest or next nearest lymph glands are generally converted into indolent buboes; these may, if complications are present, go on to suppuration.	An enlargement of the lymphatic glands in the neighborhood of the ulcer does not occur in the greater number of cases; if it should take place, however, it will increase quite rapidly to a suppurative lymphadenitis; the pus is frequently inoculable.
If the lymphatic vessels leading from the initial lesion to the indolent buboes are also affected by the syphilitic virus, they are changed into hard, knotty, painless cords, which quite frequently can be discovered only by the touch. These sclerosed lymphatic vessels less frequently than the buboes go on to suppuration.	The affection of the lymphatic vessels, which is a less frequent accompaniment of the venereal ulcer, presents the picture of an acute lymphangitis: red stripes make their appearance in the skin, corresponding to which the painfully swollen lymphatic vessels are found in the deeper parts; suppuration is not very rare. The pus coming from these abscesses may be inoculable.

It stands to reason that this table of the clinical characteristics which distinguish the venereal ulcer from an initial lesion, must in exceptional cases be supplemented by the description previously given; in this I have especially had in mind the syphilitic chancre which develops together with a venereal ulcer. When the initial lesion is not very well marked, or its character is obscured by complicating inflammatory processes, a diagnosis can be made only after a more prolonged observation.

Before leaving the subject of the initial lesion, I will relate the history of a very rare case in which a carcinoma developed on the site of a former syphilitic chancre. Carcinomata originating from gummata or accompanying gummata have been observed several times by myself and others, as we shall see later, but there are only two authentic cases reported, so far as I know, of a cancer developing from a primary syphilitic lesion.

The patient was a man, 32 years of age, who was under treatment in 1888 (from the end of February to July) in my clinic, suffering from an induration which had its seat on the inner surface of the prepuce; he had also a number of venereal papillomata here and there, lymphadenitis suppurativa of both groins, and an exanthem. The papillomata were destroyed with caustic lead, the abscesses of the lymphatic glands were incised and curretted, and oleum cinereum was given for the constitutional affection. The patient left the hospital perfectly cured. In March, 1888, the man again made his appearance; there was no trace of syphilis present; linear scars could be seen in the groins; the left half of the inner surface of the prepuce was the seat of a carcinoma, which involved the neighboring portion of the glans penis and had already occasioned destruction here. The patient was afterwards (March 26th) operated on in Billroth's clinic, and soon after submitted to three successive operations (December 4th, 1889, January and February 19th, 1890), for removal of carcinoma of the groin and its neighborhood.

A similar case was reported by I. Doutrelepont, who observed a carcinoma in a woman thirty years of age, which had originated in an indurated chancre of the right labium; the patient died from a recurrence at the age of thirty-four years.

CONSTITUTIONAL SYPHILIS.

Up to the present time we have not arrived at a common understanding as to how soon after syphilitic infection the virus shows its constitutional effects. In the earlier authors we not infrequently meet with the statement that immediately after the infectious matter is inoculated an alteration of the general condition takes place, and in our own day this view does not seem to be fully abandoned. The belief of most syphilologists at present seems to be that we cannot expect any constitutional effects until the appearance of the initial lesion which is formed at the point of entrance of the virus. With the appearanco of the initial lesion, however, constitutional syphilis, according to some, is already present, so that the first changes at the point of infection may be looked upon as one symptom of the constitutional disease; but the great majority are of the opinion that the initial lesion is a purely local process, which is followed after another interval by constitutional symptoms.

This disputed point can be settled only after our knowledge of the syphilitic virus and its biochemistry has been established on a solid foundation. But as we know as yet so little of the life history of the syphilitic virus, we must try to learn its nature from the changes which it produces in its host, man. And first we may remark that, according to clinical and histological experience, there is no

doubt whatever that the deposited virus excites a cellular new formation at the place of infection, which constitutes for the most part the characteristic induration of the syphilitic initial lesion. This cellular new growth may possibly act for some time as a barrier between the point of infection and the healthy tissues surrounding it. The great part of the virus is in all probability enclosed in the tissue cells, but some part of it may also lie free in the tissues.

In the first case, which seems to me the usual one, the virus is carried along by the cells; when the virus lies free in the tissues it may spread by independent movement (at least such would be effected by its growth); but in either case the lymphatic and the blood channels must not be forgotten.

If now the newly formed cells, which originally acted as a barrier, begin to migrate, the first impulse is already given to the spread of the virus, which may then continue in various ways.

We have already mentioned the migration of the virus from the initial lesion, that is to say, from the point of infection, through the lymphatic vessels to the neighboring lymphatic glands. We are certainly also justified in assuming that the virus may directly enter the blood current from the point of infection, although this form of extension does not seem to occur frequently. Now since the virus carried into the lymph channels, after a certain period of quiescence, finally enters the blood circulation, that is to say, the general constitution, we must admit the possibility of a nearly immediate generalization of syphilis, when the virus enters the circulatory system directly from the point of infection.

Besides this we have still two forms of extension to consider, which occur before lues becomes constitutional, and which may therefore lead to *intermediary* syphilitic products. One of these forms until now seldom, almost never, indeed, observed, is extension through the interstices of the tissues, whether the virus possesses an inherent power of change of place, or whether it is taken up by migrating cells and carried onward.

We are forced to accept this mode of extension by the observation that, in some cases, soon after the appearance of the initial lesion, although this is covered with an intact epithelium, and before the outbreak of constitutional symptoms, *macules* or small *papules* appear in the immediate neighborhood, and these, considering the time of their appearance, cannot possibly be looked upon as a sign of constitutional trouble, and can therefore scarcely be due to anything else than a *regional infection.* I am perfectly convinced of the actuality of these *regional migrations* of the syphilitic virus, from my own clinical observations. In men, small papules are not infrequently found on

the glans or on the skin of the penis some time after the appearance, and in the neighborhood, of the non-eroded initial lesion. In women, the papules which are observed in the neighborhood of the initial lesion, during the existence of an intact initial lesion, and previous to the occurrence of constitutional symptoms, may in many cases have been the result of this regional migration. The second form of extension previous to the constitutional effects of syphilis is undoubtedly by inoculation of the virus in places in the immediate vicinity of, and also more remote from, the initial lesion. Inoculations of this kind are called by me *postinitial infections;* we can understand that these are possible only when the primary lesion is denuded. In those cases in which we find well-characterized initial lesions on the genitalia, and at some distance from them, a contemporaneous infection may have occurred, the possibility of which has been proven by observations by myself and others. In many cases, however, the evidence is most strongly in favor of a post-initial infection.

Clinical examples of the appearance of intermediate syphilitic products or postinitial manifestations have been reported by A. Haslund, Karl Ullmann (from my clinic), and Otto Lasch (from Neisser's clinic). Postinitial infection on the arm, the thigh, or other part is not so very rare in cases in which, while syphilis is still fresh, the patient suffers from excoriations, scabies, folliculitis, or any other process accompanied by a loosening of the epidermis. The possibility of postinitial infection has been proved beyond doubt experimentally. In a number of patients who were affected with an initial manifestation, Pontoppidan obtained typical initial lesions by inoculating distant parts (abdomen, arm). Otto Lasch also reports cases belonging to this category.

We must, therefore, take into account the fact that the virus of syphilis, before the disease becomes constitutional, may reach localities more or less distant from the initial lesion, not alone through the lymph channels, but also by regional migration or by postinitial infection. It may be well to mention that, in cases in which the initial lesion is deprived of its epithelium, all three forms of propagation are possible, while the initial lesion which is covered by epithelium excludes propagation by postinitial infection. These clinical and experimental researches with postinitial infection, therefore, make it absolutely certain that a person does not become constitutionally diseased immediately after infection, and that even after a manifest development of the initial lesion and distinct involvement of the neighboring lymphatic glands a constitutional effect of the virus is not necessarily present.

In all probability this intermediary period varies in different individuals; as a general thing we may assert that, if the constitutional infection occurs through the lymphatics, it may last fourteen days or even longer, while it will be greatly reduced in cases in which the virus directly enters the blood (veins), and occasionally it does not take place at all.

The constitutional effects of syphilis, as has been mentioned, are no doubt dependent upon the final transportation of the virus (in all probability through the intermediary of the lymph channels) by way of the circulatory system to all parts of the body; and in fact there is no physiological tissue, no part of any organ known, in which syphilitic pathological products have not been found. With this we must, however, also confess that some portions of the human body show a certain undoubted predilection for the syphilitic process. Although in the vast majority of cases the first signs of the constitutional effects manifest themselves on the cutis, we must nevertheless remember that the skin may now and then show hardly any changes, and the mucous membrane will then take its place as the portion mainly affected; the possibility of disturbances within the nervous system, the osseous system, or of any deeply situated or visceral structures, even before the skin and mucous membranes have shown any marked changes, should, moreover, be borne in mind, and these disturbances are to be looked upon as an expression of the constitutional affection. We should, therefore, remember that, contrary to the asserted belief of Ricord, there is no law as to the order of appearance and the gravity of the syphilitic manifestations.

Ricord taught, as we know, that the constitutional effects first became manifest in the superficial and later in the deeper (internal) organs and tissues, and he accordingly introduced the seductive terms, "primary," "secondary," and "tertiary" syphilis—expressions which are still in use at the present time, and which result merely in confusing the inexperienced and the less well-informed. We cannot, therefore, sufficiently emphasize the fact that in reality this regular sequence does not always occur. If we, therefore, in the following pages treat of the diseases of the various organs and tissues in a certain order, it is understood that this is done only as a matter of convenience.

After the existence of the initial lesion for a shorter or sometimes longer period, we will hear some patients complain of manifold disturbances, such as "rheumatic pains" in the extremities, general malaise, a dull feeling of the head, disgust for work, disturbed sleep, etc., no objective changes being anywhere discoverable. It seems beyond question that we must look upon such manifestations as the

first symptoms of a constitutional effect, in particular, however, as the beginning of some irritation, which is to be ascribed to the effects of the virus already circulating in the blood, or of its metabolic products on the central nervous system or its membranes. In individual cases such an early irritation of the meninges (or the nerve centres) may be demonstrated with a certainty that cannot be gainsaid.

It should, however, be emphasized that a large number of those who have contracted an initial lesion will be spared any other manifestation until a constitutional syphilide appears, or to within a few days of this time.

Syphilitic Fever.

As we have already explained, we must assume in syphilis, as well as in other contagious diseases, a contagium vivum as the causa morbi; as, however, in scarlatina, variola, etc., fever makes its appearance as a result of the entrance of the suspected microorganisms into the fluids of the body so we observe a similar effect after a large quantity of the syphilitic virus has entered the blood. We shall designate this fever, which as a rule precedes the constitutional invasion of the syphilitic process, as the *fever of syphilitic invasion*. At the same time it is a matter of perfect indifference whether the fever of invasion is due to a chemical product which arises from the metabolism of the supposed microorganism, or whether the virus after entering the blood produces products of disintegration in the latter, which usually lead in themselves, as we know, to fever.

The virus stored in the initial lesion and in the lymph glands seems, however, also to enter the circulation in successive instalments; it can at least be observed that the eruption of recent constitutional syphilis is in many individuals ushered in by fever. Very often, however, the symptoms of constitutional syphilis make their appearance when no febrile symptoms can be demonstrated either objectively or subjectively; in these cases the probability exists that the migration of the virus into the fluids of the body is distributed over a longer period of time, and taking place so gradually is not observed. We must, therefore, conclude from the clinical symptoms that the passage of the virus into the blood either takes place gradually or that larger quantities enter the circulation at once, or in several distinct instalments.

It may perhaps be concluded, from the fact that the constitutional symptoms of syphilis are sometimes ushered in with fever which may occasionally attain a high degree, at other times without pyrexia, that in the latter case we have simply to do with individuals who have a lowered irritability of certain nerve centres. At present it is

impossible for us to say which form of syphilis will pursue a mild course and which will become severe.

In how far the high temperature of the fever of invasion is destructive to the virus of syphilis, rendering the course of lues milder, we cannot say. On the other hand, I as well as others have frequently observed that intercurrent febrile diseases, such as pneumonia, erysipelas, smallpox, typhoid fever, or acute articular rheumatism, occasionally exert an extraordinarily favorable influence on the syphilitic process.

It is necessary to distinguish the fever of invasion, which occasionally marks the beginning of the constitutional affection, from that which is usually observed in the later course of the constitutional affection, in extensive osseous or muscular disease, grave eye affections, and in processes accompanied by suppuration and disintegration, such as pustular and ulcerative processes, etc.; in the latter cases, which are very numerous, it is likely that the fever is not so much due to the action of the syphilitic virus as it is to that of the common pus cocci.

Although the virus may at certain times be equally divided in the circulating fluids, the abnormal irritative condition of the vessels in general, and of the cutaneous vessels in particular, which exists during the fever of invasion, will greatly influence the final quantitative participation of individual organs and tissues. It is possible that the increased irritability of the vasodilators or the lowered function of the vasoconstrictors may play a foremost rôle here, inasmuch as dilated vessels as a rule permit a larger quantity of their contents (carrying the virus) to transude.

We have already stated that in the later stages of the syphilitic process pathological changes are to be looked for only in those places where the virus was deposited after the first invasions, so that there would seem to be a certain regulatory effect, as respects the distribution of the syphilitic virus in the individual, in the fever of invasion.

We are, however, not yet in possession of a sufficient number of observations to show us why syphilitic affections of the internal organs occur more rarely, or in less pronounced degree, in individuals who have had, at the time of the generalization of the disease, a copious eruption on the skin and mucous membranes. It is to be hoped that now, after attention has been once called to this matter, researches in this direction will be made, and perhaps a beginning has already been made as regards cerebral syphilis, for a number of authors of high reputation as syphilologists have called attention to the fact that the greater number of patients who present cerebral

symptoms of syphilis have suffered from an unusually small number of cutaneous syphilides. There are, however, other important factors to be considered in connection with this phenomenon. Physicians have long noticed the fact that the fever which accompanies the development of constitutional symptoms usually presents a certain type (Frank Stoll). Ever since thermometrical observations began to be made in cases of syphilis, the remittent character of the fever has attracted the attention of all syphilologists and has been carefully studied by them (Wunderlich).

Although suppuration and the products of disintegration occurring in the course of syphilis quite frequently influence the character of the fever, it is nevertheless probable that the later processes also are accompanied by a specific syphilitic fever, for which the preparations of mercury and iodine are looked upon as the best febrifuges. The *fever of invasion* which we have described will, however, nearly without exception retain the character of a purely syphilitic fever. This fever usually makes its appearance, when it is at all marked, from seven to eight weeks after the infection. From this we may draw the conclusion that, with certain exceptions, the passing of the greater quantity of the virus into the blood current and together with it the appearance of the constitutional effects of syphilis occur about seven or eight weeks after infection. The constitutional affection has, however, been observed much earlier, even in the fourth week, and occasionally also much later. In one of my patients the first slight traces of a roseola were not observed until one hundred and thirty days after infection; eight days later the syphilide was plainly marked, the tonsils being also covered with mucous patches. In a woman who had a primary induration on the lip, the first symptoms of a constitutional affection occurred five months after infection. R. Bergh reports several cases of this kind. The fever of invasion is also designated syphilitic fever of eruption, for the reason that the appearance of an eruption on the skin or mucous membrane rarely remains absent after its occurrence.

The fever is very seldom ushered in by a chill; as a general rule it makes itself felt by headache, malaise, general depression, weakness of the knees, and quite frequently rheumatoid pains; anorexia or possibly an insatiable appetite is complained of; in individual cases the pain assumes a neuralgic character. Together with these subjective symptoms, which are especially painful in the afternoon or at night, we note an increase of the temperature to 40° C. (104° F.) or even sometimes to 41° C. (105.8° F.) or over in the evening, with morning remissions reaching nearly to normal. This fever lasts two, three, or four days, rarely longer; after it has existed for a day or

two, a faint diffused blush is observed here and there on the trunk; but this rapidly disappears to make way for the eruption of the true cutaneous syphilide, which is due to a hyperæmia and a more or less pronounced infiltration; it also occasionally makes its appearance on the mucous membranes. The subjective symptoms continue for a considerable period, perhaps one or two weeks, in rare cases only as a rule they will have already begun to diminish before the eruption makes its appearance and will soon disappear altogether; the temperature begins to fall only after the eruption has appeared, but defervescence seems to be complete one or two days later.

Although the syphilide continues to increase during the following days and weeks, by the appearance of successive eruptions on skin or mucous membrane, this as a rule occurs without any febrile symptoms whatever. A fever of pronounced remittent type lasting a day or two is, however, quite frequently observed as an accompaniment of subsequent eruption as well as of recurrent skin and mucous-membrane syphilides. Such a fever never reaches the height of the fever of invasion.

CUTANEOUS SYPHILIDES.

The syphilitic affections of the general cutis, the skin syphilides, according to our present knowledge appear to be but little influenced by the presence or absence of a fever of invasion.

Entirely independent of the latter, the body may be found fully covered with an exanthem, at times presenting only a few lesions, which may besides be so indistinct that their true nature, when the other symptoms are ignored, may under certain circumstances become very difficult.

Location.—The syphilitic skin eruptions are scarcely ever equally distributed over the whole body, on their first appearance. The trunk is most usually affected, after this the scalp, and then one or another of the extremities; when the latter are attacked the thighs and arms are as a rule more affected than the legs and forearms, the flexor more than the extensor surfaces; accordingly the palms of the hands and the soles of the feet are the favorite seats of the early form of the disease, the dorsa of the hands and feet being more rarely affected at this stage.

In addition to these, I might say daily, occurrences, many other peculiar methods of distribution are also found. In one case the syphilide occupies by preference the anterior, in another the posterior half of the body; in one case we find that the exanthem occupies only one zone of the trunk (having a distant resemblance to a bilateral zoster), while in another individual it is confined more to the shoulder

or more to the pelvic region; cases in which the syphilitic exanthem is met with mainly on the upper or mainly on the lower half of the body are also by no means unique. No matter how the cutaneous eruptions are distributed, however, they will be found (we are referring now to a primary eruption) equally on the right and left sides in the great majority of cases.

In rarer cases we note the occurrence of isolated lesions a few days (from ten to twenty) before the full eruption of the syphilide, these constituting as it were an advance guard; the preliminary eruption in these cases usually consists of one or more isolated papules.

In a few individual patients of my own, two livid patches of roseola, the size of a half-dollar, developed on one side of the thorax and remained unchanged for a long time, disappearing only along with the general cutaneous syphilide (which came on about two weeks later) as a result of constitutional treatment. Obviously in this case only very small quantities of virus passed into the circulation previous to the general invasion.

In exceptional cases the first eruption confines itself in general to single symmetrically distributed efflorescences.

Varieties.—Before entering upon a detailed discussion of the morbid changes of the general integument, which make their appearance in the course of syphilis, we would emphasize the fact that probably all forms of lesions which are observed in non-syphilitic dermatoses may occur also in syphilis, but that some of these, as vesicles with clear contents or the pigmented and squamous lesions, very rarely occur as primary eruptions, other lesions usually having preceded them. Most frequently roseola spots and papules, and quite commonly pustules are observed, as also gummatous infiltrations of the skin and subcutaneous tissues.

Characteristics.—The cutaneous syphilides are distinguished by a whole series of characteristic marks.

The efflorescences of syphilis stand out more distinctly from the surrounding normal skin, and consequently seem more sharply defined, than their vulgar sisters of the same name. The reason for this in all probability lies mainly in the fact that the syphilitic eruptions do not possess the inflammatory areola which so frequently surrounds the ordinary exanthem. Equally sharp demarcations of the diseased portions are, however, regularly found in dermatomycoses, and occasionally in erythema and other cutaneous affections, and consequently these may readily be confounded with cutaneous syphilides.

The redness of the syphilitic efflorescence is vivid only in the early period; after it has existed some time it fades to a dark bluish-red or dirty brownish-red and then remains stationary for some time. The

older syphilitic efflorescences are also apt to remain for some time in the same condition, while the non-specific eruptions change more rapidly.

With few exceptions the ordinary cutaneous eruptions are distributed symmetrically over the body, while only the earlier forms of syphilitic eruption observe a symmetrical distribution; the recurrent eruptions are especially noted for their asymmetry; while the grouped eruptions frequently present a circular or bowshaped form—the so-called serpigines.

Certain cutaneous areas in which non-specific eruptions frequently make their appearance are not the favorite seats of syphilitic eruptions, and *vice versa*. The syphilitic eruptions, with the exception of some painful gummata, are as a rule not accompanied by itching, burning, or other distressing sensations, unless they occur in places which are stretched and distorted by movements, or are macerated by physiological and pathological secretions; as a result we will very seldom observe the marks of scratching in their neighborhood.

In rare cases hemorrhages will be found in the vicinity of syphilitic efflorescences (syphilis hæmorrhagica). The cutaneous syphilides are very frequently accompanied by affections of the mucous membranes, which is not so often the case in the non-syphilitic dermatoses.

Roseola Syphilitica.

In taking up the description of the individual cutaneous syphilides, we shall begin with roseola, for the reason that it occurs most frequently as the first objective symptom of constitutional syphilis, produces the least marked changes in the skin, and sometimes represents the preliminary stage of other efflorescences. Roseola syphilitica (syphilitic erythema, macular syphilide, Flecksyphilid) occurs in the form of red spots of the size of a pin's head to that of a lentil or a fingernail, more or less elevated above the surface; they may appear at once as such or may be developed from evanescent, scarcely visible pin points of erythema. In the first few days only a few spots are visible; but they increase rapidly and by the end of a week they have usually attained their full number. The efflorescences consist, as clinical observation has shown us, not only of hyperæmia, but also of an infiltration of the tissues; for the redness does not always disappear entirely on pressure, and the palpating finger will frequently distinguish, even in those cases in which the spot is not visible above the level of the skin, a marked difference in consistence between the roseolar efflorescence and the healthy integument surrounding it. In a deeply pigmented skin, the clinical characteristics of roseola are less distinctly marked.

Pathological Anatomy.

An anatomical examination of roseola syphilitica reveals an increase in the nuclei of the capillaries; in the perivascular lymphatic spaces a copious cell formation and proliferation of the adventitial elements of the larger vessels which run towards the papillæ, and proliferating connective-tissue corpuscles in the latter; also pigmented exudation cells and vegetations around the hair follicles, sebaceous follicles, and sweat glands. In some cases the infiltration of roseola is so distinctly marked that most of the spots appear as broad, flat, erythematous elevations, and justify the term, *maculopapular syphilide.*

Symptoms.

The roseola spots, which may, like any other syphilitic efflorescence, occur in any locality, appear with greatest frequency on the trunk; when the eruption is very thick, it may be observed extending to the arms and thighs, and in still more severe cases it may also occupy the forearms and legs, in which case the palmar surfaces of the hands and soles of the feet are usually also affected by the disease. Roseola spots are only rarely met with on the backs of the hands and feet. In exceptional cases, however, especially in individuals who lead an irregular life and in whom syphilis as a general rule assumes a graver form, we find the roseola distributed over the entire body in such a manner that we are unable to find anywhere, even on the head and face, any considerable area of healthy skin; isolated efflorescences may even be seen on the back of the hands, which usually remain unaffected.

When left to itself, this syphilide disappears occasionally at the end of a very short period, but generally it persists for quite a time, retaining its bright color for one, or at the most two weeks; the infiltration then gradually diminishes, its color approaches more and more to the normal, passing through a dirty brown and dirty gray, until after three or four weeks more, the syphilide will have disappeared without leaving a trace behind, except such as we shall shortly mention.

We are, however, occasionally confronted by a syphilitic erythema which, instead of running its course in the average time of a few weeks, or the extremely short period of only a few days, persists for months; in that case distinct pigmentations will remain behind for some time on the site of the efflorescence, and some of them may even desquamate during their involution. At other times the whole proc-

ess is very greatly prolonged by the fact that new crops of roseola constantly appear in fresh localities.

Although roseola syphilitica does not usually lead to other changes in the skin, even after it has existed for months, we do occasionally meet with certain morbid changes resulting therefrom, which are worthy of attention. We may find here and there on the trunk groups of very small nodules which take the place of the vanishing spots of erythema, and which, except for their dirty brown color, resemble the efflorescences of lichen scrofulosorum. If the roseolar eruption occurs in a locality which is rich in sebaceous glands, an increased secretion takes place from the glands, and this forms with the superficial layers of the epidermis a dirty brownish scaly crust. These fatty *impetigo crusts*, adherent to a dirty brownish-red and somewhat infiltrated base, will be most distinctly seen on the hairy scalp, especially at its borders on the forehead and neck, in the nasolabial fold, on the chin, the external genitals, etc.

As regards the appearance of the syphilitic erythema on the *genitals*, we must, however, add that, if this is seated on parts where the secreted sebum is kept moist and becomes decomposed, and so macerates and (from the presence of pathogenic microbes) irritates the site of the efflorescences (as is the case in the prepuce or on the vulva), we may also find a catarrhal condition, particularly a *balanoposthitis* or *vulvitis*. If the roseola has already disappeared from the rest of the body, or we are dealing with a recurrent syphilitic erythema which affects only the glans or the vulva, we may very readily mistake it for a simple, non-specific balanoposthitis or vulvitis. In cases of this kind in which the initial lesion has been overlooked, it may seem incomprehensible that symptoms with indisputable syphilitic characteristics should follow a gonorrhœal inflammation of the glans penis. On close inspection of these cases, however, we shall find that while the diseased part, for example the glans, may be reddened over its whole surface, nevertheless the accompanying erosions correspond mainly to distinctly circumscribed flat infiltrations, and that we are dealing with a syphilitic blennorrhœa of the glans in the true sense of the word, as the secretion is mainly caused by syphilitic efflorescences.

On hairy parts, loosening of the hairs occurs in the hair follicles, which is perhaps the result of an overproduction of the epithelial elements beginning in the sebaceous glands and extending to the root sheaths, and we then find a defluvium capillorum corresponding in area of the circumscribed cutaneous affection. As a rule this loss of hair occurs only on spots the size of a lentil to that of the end of the finger; in rare cases these small islets of alopecia coalesce and form

large bald patches. This loss of hair is most frequently observed on the head, but it is not very unusual to meet with it in the eyebrows, the axillæ, the pubes, etc., or even in all of these places at the same time.

Other lesions may also appear during the existence of the roseola, individual macules showing in their centre smaller or larger infiltrations, forming nodules or papules, a few of which persist for some time and may outlive the macular syphilide by some weeks. These papules may indeed occur on any part of the skin, but they are most frequently met with in the axilla, the bend of the elbow, under the mammæ, at the umbilicus, on the external genitals, in the groin, or in the popliteal space.

Affections of the mucous membrane and a universal swelling of the lymphatic glands quite frequently accompany roseola syphilitica; more rarely we find slight meningeal and joint affections, periostitis, iritis, infiltration of the testicle; acute nephritis, enlargement of the spleen, and affections of other organs may also, though rarely, be observed complicating this syphilide. I once saw typical epileptic seizures occurring suddenly in a young man twenty-three years of age, who was under treatment for an ulcerating chancre and a maculopapular exanthem; the convulsions had never occurred previous to the infection, and no hereditary syphilitic taint could be detected. Another patient, twenty-one years of age, suffering from an ulcerating chancre and a recent maculopapular syphilide, was seized with clonic spasms of the extremities, and with loss of consciousness before constitutional treatment was instituted; after a course of injections of oleum cinereum (see the section on Treatment) the spasms disappeared.

When these complications are absent, the macular syphilide, except during the eruptive stage, which lasts at the most a few days and the symptoms of which may be almost unnoticeable, causes so little trouble that we can very well understand how it frequently escapes the notice of the patient, or even that of a not very observant physician.

Recurrent Roseola.—As we have already mentioned, syphilis may come to an end in any stage, therefore also with the roseola; or it may offer repeated proofs of its vitality in fresh attacks, and this recurrent syphilis may assume the appearance of a roseola. The recurrent lesions may perfectly resemble those of the first eruption, but as a rule the individual maculæ are larger, livid, and more markedly infiltrated than those of the first attack; sometimes we find them seated chiefly on the shoulders and the anterior or posterior folds of the axillæ. Sometimes involution, which is generally slow, begins in the centre of the patch, and circular lesions are then left—*syphilis*

annularis, roseola annularis—which, spreading out at the periphery and healing at the centre, form wider and wider circles, and where they overlap make neat figures—*roseola serpiginosa, gyrata, aut figurata.* These recurrences, which make their appearance many months, perhaps one or two years after infection, or even later still, are frequently met with only in single asymmetrically distributed lesions which are frequently squamous.

Diagnosis.

As we usually find the initial lesion with its accompanying indolent buboes present at the same time with the syphilitic exanthem, and frequently also other attendant symptoms, this syphilide is as a rule readily recognized as such. Under certain conditions, however, mistakes may be made, and attention should be paid to the following points in the differential diagnosis.

We need not confound roseola syphilitica with *measles, roetheln*, etc., if we bear in mind that very high fever is present or precedes the acute exanthemata, even in their lighter forms; that the eruption is especially marked in those localities (head and face) where the syphilitic erythema does not usually occur; that the individual lesions are surrounded by extensive hyperæmic portions of skin; that acute affections of the mucous membrane occur, etc., etc.

The inexperienced would be more likely to mistake a *roseola balsamica* for a syphilitic erythema, and especially because this drug eruption, which usually makes its appearance in patients suffering with gonorrhœa who are taking balsams for therapeutic purposes, might arouse the suspicion that a concealed initial lesion coexisted with the gonorrhœa. The differential diagnosis will, however, not be difficult if we recollect that roseola balsamica also frequently presents urticarial lesions (*urticaria balsamica*), which may form great wheals as big as a Vienna roll in portions of the body which are subject to pressure (as the nates in sitting), or are irritated in any way (by garters, cuffs, etc.); that the eruption itches greatly, or may even cause a burning sensation, and that it gradually subsides when the administration of the drug is discontinued.

Occasionally a *tinea versicolor* may be mistaken for a roseola syphilitica undergoing involution. If we pass the finger nail with a rapid firm movement over the diseased portion of skin, the cutis will be removed in shreds in the case of tinea versicolor, in which we may easily discover the microsporon furfur under the miscroscope. In cleanly individuals who bathe frequently these shreds are not so easily obtained.

Hardly any difficulty is experienced in distinguishing *erythema iris* and *annulare* from a syphilitic erythema, as the former is seated chiefly on the backs of the hands and feet, localities which are usually spared in roseola syphilitica; furthermore, the erythema disappears in about two weeks, even without any treatment whatever.

If a recurrent roseola syphilica is present in the form of plaques, rings, or convolutions accompanied by only slight desquamation, the resemblance to *tinea circinata* (*tonsurans*) is frequently very deceptive, but the detection of the trichophyton in the scales (and hair) will suffice to establish the diagnosis.

I have several times seen persons convalescent from *smallpox* who had hardly any visible changes on the face, but presented very delicate, superficial, distinctly circumscribed, and finely lined *cicatrices* of the size of a finger nail on the trunk, the nates, or in other places, and through which showed a faint red color, due to the layer of vessels beneath. On superficial observation, these give the impression of circumscribed maculæ, and I have actually seen the mistake made, the patient being subjected to a mercurial course, under the belief that the eruption was a syphilitic roseola.

Many persons infected with *pediculi pubis* present on the trunk or the thighs *steel blue maculæ* from the size of a lentil to that of a glove button, which may very easily be mistaken for roseola lesions. These spots, known since the time of Mourson as *tâches bleues*, evidently are a sort of erythema toxicum, caused by the secretion of the pediculus pubis. In these cases we shall very frequently find the eggs (nits) adhering to lanugo hairs in the neighborhood of these blue spots; but the discovery of the insect itself in its characteristic location (pubes, etc.) will make the diagnosis certain.

We should also mention that under certain conditions (as the expression of a temporary or permanent angioneurosis) a dilatation of the smallest cutaneous vessels occurs, and we then find bluish spots covering larger or smaller areas, or a wine-red network, *cutis marmorata livida*. Such spots do not, of course, show a trace of infiltration. If they are due to the action of cold they will disappear in an equable temperature; if the angioneurosis is permanent, however, the markings will remain, but no sign of evolution or involution (such as occurs in luetic efflorescences) will be observed.

Papular Syphilide (Syphilis Papulosa).

We have already mentioned under the heading of the macular syphilide that a papular form of the affection may in rare instances be developed from the roseola efflorescence, by increasing infiltra-

tion. Here and there any of the efflorescences of the primary eruption may, however, assume a papular form, and in this manner the papular syphilide may become the first symptom of general infection. It frequently follows a roseola.

The eruption of the papular syphilide also may be preceded by a slight eruptive fever. Two or three days later hyperæmic spots from the size of a pin's head to that of a lentil make their appearance over the whole body, lying close together in certain localities and coalescing so as to form an extensive erythema. These present after a few days infiltrations, papules, of a pointed semiglobular or flat form, raised above the level of the skin, ranging in size from a barleycorn to a pea and even larger. At other times these papules may make their appearance without any previous hyperæmia or other changes of the skin.

An anatomical examination reveals a new cell formation arising from the connective tissue, but especially from the walls of the vessels, which is present not only in the papillary layer but also in the deeper layers of the cutis, and even extends into the subcutaneous connective tissue. Quite frequently this new growth is found to be most dense in the neighborhood of the hair follicles and of the sebaceous and sweat glands. The new growth of the walls of the vessels in the upper layers of the cutis also contains pigment. Besides this, arteritis obliterans is also likely to occur.

These glandular formations frequently remain unchanged for a long period, at least I have repeatedly not only seen follicular and convoluted glands well preserved, but have also been very well able to trace their excretory ducts to the surface of the papule. The greater the infiltration the more will the newly formed cells also penetrate into the stratum Malphighii and will finally obliterate the boundary line between the latter and the papillæ; in a much greater degree the newly formed cells will have wholly replaced the rete Malpighii, and extended to the free surface. This is obviously the initial step of a breaking-down process, for which very likely the arteritis obliterans, which is observed accompanying it, is responsible.

According to the size of the nodule, we distinguish between a small and a large papular syphilde, or a miliary papular syphilide and a lenticular papular syphilide. With this we observe that the larger efflorescences appear at once of full size, or else they are formed in the course of time from the smaller lesions, or they are developed from the roseola macules. The eruption, however, presents manifold variations in addition to these.

As regards the color of the syphilitic papule, its red tint is rarely, and then only during the first few days, of a bright hue, and it gives

place later to a mixed shade of dark blue or dark brown color. At times the efflorescence, however, becomes so pale that it only very slightly differs in hue from its surroundings. The further development of the papule is variable, according as it is situated in a dry region or in one which, by reason of the anatomical conditions, is moist and warm. Thus we observe, in most localities of the trunk, on the extensor surfaces of the extremities, and in other dry situations, that the papules do not grow larger than the size of a pin head or a lentil, as a general thing not larger than a pea, are but slightly scaly, and, as a rule, remain dry.

When a dry papule begins to retrograde, the red color and the infiltration disappear, and desquamation also takes place on the surface of the lesion; the papule in this manner becomes smaller and smaller, until it seems after a few weeks to have been totally absorbed, and the round place where the papule had existed is now marked only by slight desquamation. Gradually this also disappears, and every trace of a former affection is then gone. Should, however, infiltration and hyperæmia persist for a longer period, we may note, besides the desquamation, a dirty bluish-red, reddish-brown, or gray discoloration, and in this case it is quite likely that the coloring-matter of the blood has transuded into the hyperæmic tissues and become deposited there, where it is changed into pigment. In cases of this kind we are also able, for a long time after the papule has been wholly absorbed and when desquamation has also ceased, to recognize a dark blue to gray spot of pigment at the point where the papule had been. This pigment will, however, also be absorbed after a few weeks, the absorption extending even to the normal pigment of the stratum Malpighii of this location, which will then present a total absence of pigment and bear witness as a light spot for many months or even years to the former presence of the papule (see also "Leucoderma," below).

On the whole, the lenticular papular syphilide, which is usually of more benign course, is most frequently met with. The lenticular papules are usually found symmetrically distributed over the above-mentioned parts as the first expression of general infection or as an early recurrent form.

This syphilide is usually absorbed within a few weeks in the manner above described. Only in neglected cases it may last for a longer period, even for months, when the individual efflorescences occasionally reach a notable circumference.

Occasionally the first expression of syphilis manifests itself in the form of only few very large papules, from the size of a pea to that of a bean (giant papules), of the color of a biscuit or the crust of

bread, which make their appearance in an altogether irregular manner on the forehead, the hairy scalp or the face, or are scattered here and there over the trunk and on the extremities. Such single giant papules, appearing as the first symptoms of a general infection, are of not very favorable omen as regards the further course of the disease. Although the patients attacked in this manner, coming under my observation, seemed to be in robust health, I could nevertheless see that in their case the syphilitic symptoms were apt to recur very early and in a grave form.

An even more unfavorable prognosis must be given in the case of the small papular or miliary papular syphilide, the lichen syphiliticus. In this syphilide the papules are of a dirty brownish-red appearance, hardly reach the size of a millet seed, and are diffusely scattered over large portions of the trunk or of the extremities, or are aggregated together in groups; as a rule they persist a long time, generally much longer than the lenticular papules. Their absorption is usually accompanied by atrophy of the skin, therefore after the healing of the small nodular syphilide a shallow punctiform cicatrix is frequently left behind. The small papular syphilide occasionally initiates the general infection; sometimes it appears with the macular syphilide, in such a manner that miliary papules make their appearance within the borders of large roseola plaques; or it takes the place of a recurring eruption, in which case the efflorescences occur partly in the manner described above, partly in the form of circles or crescents (serpigines). Not very infrequently we meet with individual lenticular papules, together with a copious eruption of lichen syphiliticus.

As we shall see later, papules may also appear on the mucous membrane; I have, however, only exceptionally found the character of the miliary papule plainly marked in this situation. It is nearly always to be observed that persons who present the miliary papular syphilide are in poor health, and are noticeable for their pallor, defective nutrition, and scrofulous habit. Accordingly syphilitic symptoms of other organs usually make their appearance at the same time (see below) in a somewhat severe form. The types of the syphilitic papule above mentioned, however, are not the only ones.

In exceptional cases, a more acute exudation occurs at the apex of the papule, which is indicated by the appearance of a very small vesicle or pustule. The stage of vesiculation only rarely lasts long enough to justify our calling it a *vesicular syphilide*, or where the efflorescences aggregate a *herpes syphiliticus*.

As a rule the fluid of the vesicle very soon dries up and the lesion forms a small scab, and in this way *impetigines* are formed; these are found with especial frequency on the hairy scalp, on the face, and on

the lower extremities—syphilitic papulocrustoses, papulopustuloses (see below). Although in this way efflorescences not dissimilar to eczema are developed, it does not seem fitting to speak of an *eczema syphiliticum*, because further inoculation after the fall of the little scab is carried on as described above, which does not occur in the same manner in common eczema, where, besides, an intense itching is also present.

Mention may furthermore be made of the fact that the syphilitic papule may, under certain conditions, also become *hemorrhagic*. I myself have noticed this in a few cases in one and another efflorescence, without the character of the disease on the whole presenting anything unusual. The hemorrhagic form, however, should always be regarded seriously, for the reason that similar extravasations of blood may also occur in vital organs (brain, etc.) and become highly menacing to the patient.

It does not seem necessary, in speaking of this symptom, to do more than refer to the changes in the blood-vessels in the course of syphilis, which will be treated of later on.

It is not so very rare to meet with a papular syphilide on the extremities or the face, which during its involution remains exceptionally long in the stage of desquamation, so that we may very well speak of a *papulosquamous syphilide*. Occasionally the squamous character predominates, which has induced a few clinicians to speak of a *squamous syphilide;* there is nothing to be said against this, it is true, but we should remember that we are here only dealing with a form of the papular syphilide.

Once only have I been in the position to see an eruption not dissimilar to psoriasis vulgaris, in a patient whom I had myself treated twelve years previously for a recent syphilis, and since then also for relapses. The efflorescences, distributed pretty equally over the whole body, of variable size, occasionally healed in the centre, were situated on a very slightly infiltrated and reddened base, and were covered only by a thin layer of small pale brownish scales; they could thus plainly be distinguished from ordinary psoriasis. We were, therefore, dealing with a syphilide which in all probability might have been from the very first in a squamous form; however, after the existence of syphilis for twelve years it cannot be positively denied that the papular may have preceded the squamous form. We shall only mention, in passing, that the squamous syphilide disappeared under an antisyphilitic treatment, and that improvement took place in the syphilitic involvement of the liver and the breast, which existed at the same time. According to their site the papules are liable to assume many other forms besides those described above.

The palms of the hands, as well as the plantar surfaces of the feet, are only in rare cases the seat of raised papules; these surfaces as a rule present but a circumscribed erythema, and almost perfectly flat infiltrations, of the size of a lentil to that of a glove-button, so that only the very slightest elevation of the skin can be noticed.

In their further course, especially when the erythema and the infiltration begin to disappear, the diseased portions become noticeable because of desquamation. The respective parts are then slightly reddened, their infiltration being recognized by the touch; they are most noticeable from the fact that they are covered in the early period by a dense adherent horny layer of epithelium, which sooner or later forms white scales; after persisting for some time, these fall off, and leave behind them a fine, thin, rose-colored skin, which is surrounded by a border of scales which are adherent at their centre and raised at the edges; desquamation of the old and accumulation of new scales alternate quite frequently on these efflorescences which reach various sizes.

Papules on the palmar surfaces of the hands and the plantar surfaces of the feet constitute at times the earliest symptoms of constitutional syphilis; they are, however, usually soon followed by eruptions on the trunk, etc.

Relapses in the form of palmar and plantar syphilides are not particularly rare; where the latter is the case the efflorescences make their appearance occasionally in crescentic forms. These papules rarely occupy only one palmar surface or one plantar surface; most frequently we find both palmar surfaces or both plantar surfaces, and quite often the two hands and the two feet affected at the same time.

The parts on the flexor surfaces of the fingers that are marked by the deeper grooves, the inner concave portion of the plantar surfaces, at times also the lateral or upper border of the heel, are the favorite seats for the papules; the distensibility of these parts of the skin on the one hand, and the brittleness caused by the infiltration and accumulation of scales on the other, afford a sufficient reason why the affection is frequently accompanied by rhagades and fissures, and may therefore be also very painful. When the palmar syphilide is very extensive, the changes extend also to the volar surface of the fingers and to the nail furrows, causing the nails to become fissured, dull, and deformed. Occasionally, even after the lapse of years, thickened portions of integument with a horny, frequently notched, epithelial layer make their appearance on individual portions of the palmar surface of the hands or the plantar surface of the feet, of the size of a pin's head to that of a lentil. Or we may find only a slight

desquamation of a somewhat thickened cutis on the fingers and hands. After the cure of a palmar syphilide which has lasted for a long time, a dirty brownish-red discoloration as a rule remains behind.

The peculiar anatomical function of the palmar and plantar surfaces is the reason why the syphilide, which locates here, only slowly passes through its stages of evolution and involution, and why the process of desquamation persists for a long time after healing of the other syphilitic products, and it also suffices to explain the term *psoriasis palmaris* or *plantaris* which has been applied to it. Not infrequently the palmar and plantar syphilide is in fact the only symptom of syphilis present; at times even a single spot on the border of the nail, or maybe elsewhere on the fingers, of the size of a pin's head to that of a lentil, horny or desquamating, may indicate to us the existence of syphilis.

The morbid picture assumes a very peculiar aspect when the papular infiltration is developed at the edge of the heel, or on some other part of the plantar surface of the foot which is covered with a thick layer of epithelium, as for example on the ball of the great toe. The cutis here presents itself, not only where the papule is situated, but also over a larger area of from 1 to 2 cm., thickened like a callus, this thickening gradually becoming less towards the outer side. The desquamation begins at the centre, so that after maceration and removal of the horny layer the circumference of the papule, still covered with an epithelial layer, can be recognized quite distinctly. In the course of the process the border of the peripheral callous ring which is immediately contiguous to the papular infiltration is lifted from its base, not, however, separating itself altogether; the lesion then resembles a gradually rising hill, resting on a broad base in whose crater-like depression a plug, having at times a smooth, at times a verrucous surface, comes to view. The whole affection in fact reminds one of a beginning perforating ulcer. If neglected, disintegration of the infiltration occurs from pressure of the callus; the ulcer thus formed shows only slight inclination to heal, on account of the callous border, and tends rather to increase in area and depth. It is a long time, even with proper treatment, before all the horny layer is removed and the infiltration is perfectly absorbed. I have also observed similar changes of the papule when situated in the palm of the hand. Unusual forms of the papule may occasionally also be seen on the face, especially on the chin and at the nasolabial fold, or on portions covered with hair, at the border of the scalp, sometimes also at the anus and genitals—as a rule, therefore, on parts rich in follicles. Here very large and succulent papules occasionally develop, which are covered with sebaceous scales or scabs, after the

removal of which the surface will be found covered with numerous papillary formations—*exuberant (frambœsia-like) papules.*

The papules present a different appearance when located on those portions of skin which, on account of their anatomical situation, are frequently moistened by physiological secretions or soiled with pathological excretion, dirt, etc. Among the places where this happens may be mentioned the external genitals, the genitocrural folds, the perineum, the anus and its neighborhood, the depression of the navel, the axillæ, and other parts of the skin which become macerated by contact; also those which are in contact with other cutaneous surfaces, such as the skin of the chest covered by a pendulous breast, and the interstices between the toes; or parts where other conditions lead to suppuration, as the furrow of the nail in cases of ingrown toe-nail, the external auditory canal in otorrhœa; and finally, all parts covered by tender epithelium, which may become irritated in some manner, as the nipple in nursing; or any portion of the integument which is soiled by urine or fæces, especially in children who are not kept scrupulously clean. The papular efflorescences which develop under the conditions mentioned above will naturally become quickly macerated and denuded of their epithelial covering, and therefore continually present a moist surface; hence the designations, *wet or moist papules, papulæ humidæ, plaques muqueuses, tubercules muqueux.* Aside from this very characteristic symptom we find still other peculiarities in the moist papules, which are due to their mode of development and retrogression.

The moist warmth of the situation in which they occur seems to favor their especially exuberant development, for while the dry papule reaches the size of a millet-seed or lentil, and as a rule does not grow larger than a pea, we find that its moist sister attains the size of a glove-button or of a silver ten-cent piece, or even a still larger size; its free surface is slightly spherical or altogether flat, and the papule is attached throughout the whole circumference of its base; from this fact have originated the names, *broad, flat,* or *shallow papules* or *condylomata lata.* The enlarged papule rises abruptly above the surrounding level, it is sometimes more, sometimes less red, succulent, and soft, and after it has existed for some time it often presents a bluish color and becomes more dry. The epithelium is either of a whitish color, as though desquamated, or else the macerated epidermal layer is very soon thrown off, and the tips of the papillæ rise as red points above the whitish interpapillary remnants of epithelium, having a raspberry appearance, excreting a copious amount of fetid pus (*pustula fœda* of the older authors).

Those portions of the skin which are kept moist and warm over

a wide extent of surface and which are at the same time soiled in careless persons, especially by dirt, such as the genital region, the anus, and their vicinity, will therefore be densely covered by these moist papules, so that the efflorescences overlap each other, leaving no normal skin whatever between them. We are able only at the edge of such a diseased zone to recognize some individual efflorescences; further on towards the centre the moist papules become flattened against themselves, so that a longitudinal or much facetted, succulent cushion covered with greasy pus is formed, in place of the flattened round formation; this is especially the case when the papules densely cover the labia minora, the perineal raphe, or other furrows covered in by the neighboring parts. The papules surrounding the anus are usually continued in swollen folds which spread around the anal orifice, assuming the shape of a leaf. In proportion as the moist skin merges into the dry, the efflorescences become less densely packed, and we find only single papules on the perfectly dry portions, which become smaller and less numerous the farther they are situated from the moist portions, and gradually take on the characteristics of the dry papules.

Should the papule, however, remain moist, a firmly adherent deposit occasionally forms on its surface, which breaks down and thus leads to a loss of substance. By a continued renewal of the deposit and its repeated breaking down, an ulcer is formed which, extending deeper and deeper, may involve gradually the whole papule, even the base on which it stands. We are then dealing with an *ulcerated papule* or a syphilitic ulcer, which has taken the place of the papule. In most cases the loss of substance in such an ulcer is confined to the area occupied by the papule, and involves at the most the whole thickness of the skin in this area. It is only in the most neglected cases that we meet with a wider destruction on the surface, or into the deeper tissues, as a result of such an ulcerated papule. In most cases the ulcer clears up and cicatrization then begins. If the parts which are naturally moist are kept dry, the purulent secretion of the free surface becomes less, maceration of the newly formed epithelium does not take place, and the latter is then thrown off in the form of small scales, as is the case in the dry lesion, and the subsequent involution is carried on in the manner already described.

In rare cases moist papules which are subjected to no treatment, in individuals who are careless as regards personal cleanliness, dry up and harden into flat, firm nodules of the same or a somewhat darker hue than the surrounding skin, and persist as permanently organized formations; in the dry papules this observation is even

more rarely made. These permanent "organized papules" are therefore more likely to be met with in localities which are the seats of predilection for moist papules, *e.g.*, the genital region or the anus; in other localities, as the angles of the mouth, they are rarely encountered.

We have seen that the papular syphilide, when it makes its appearance extensively on the skin, may assume various forms, according as the lesions are dry and scaly, as on the trunk; or covered with scabs, as on the head; or weeping and moist and very closely crowded together, as on the genitals, the anus, etc.; or else quite flat and readily scaling, at times covered by a horny layer, as on the palmar and plantar surfaces. This great variety in the appearance of the papular syphilide, occasioned by differences in location, is further increased by the fact that lesions of the same form are often found in various stages of development or retrogression.

It should also be mentioned that macular lesions may exist together with papules, whereby the polymorphism of cutaneous syphilis is still more prominently marked.

Syphilitic papules are very rarely seen on the backs of the hands and feet, or on the extensor surfaces of the extremities, but even with these exceptions an eruption of this syphilide covering the whole body occurs only during the first stages of the disease, at which time, moreover, a symmetrical distribution is very common. The seats of predilection of the papules are the trunk, the face, especially the chin and the nasolabial fold, the scalp, particularly at its margin (corona Veneris), the genitals and the parts around, the perineum and anus, the umbilical depression, the axillæ, the flexor surfaces of the hips, elbows, and knees, the palmar and the plantar surfaces, and the interstices between the toes; in some individuals there is a copious eruption of papules on the neck, especially the back of the neck. The lesions are, however, also met with in other localities, as the ungual furrow, the lids, the external auditory canal, etc.; also other parts, which are exposed to a more or less constant irritation, such as the forehead which is pressed on by the rim of a stiff hat, the bridge of the nose which is pinched by eyeglasses, or any part of the skin which is irritated by dirt, etc., may become in exceptional cases the seat of these papules.

The absorption of the papular syphilide is almost always a matter of a few weeks, though occasionally the involution does not reach its end under several months. Individual forms of this cutaneous syphilide, such as the weeping papules and those situated on the palmar and plantar surfaces, frequently remain present long after all other lesions have disappeared; at other times the process seems to be pro-

longed by the appearance in other localities of new lesions having a tardy course, while the first crop disappears.

The great danger of this stage of syphilis, which includes a marked possibility of contagion by reason of its very numerous and unusually long-persisting pathological products, is rendered still greater to the well who are brought into relations with the patient by the fact that the syphilitic moist papule, especially notable as regards its power of contagion, is one of the most frequently observed among the relapsing lesions. They are seen very frequently during the first and second year of syphilis, but the cases are not uncommon in which a recurrence of the papules is observed at a much later period.

The first relapses of the papular syphilide are occasionally preceded by an eruptive fever, and they offer also, as regards the shape and distribution of the lesions, a great similarity to the first eruption; the later the recurrence takes place, however, the less numerous are the lesions, and it not very infrequently happens that the recurring syphilis is represented by only a single moist papule, or a single desquamating or callous area on the palm of the hand or the flexor surface of one of the fingers. Occasionally we see one or two papules of the size of a lentil to that of a button, of a round or elliptical form raised at the edges like a wall, the centre being depressed and covered by a small scaly crust, or sometimes by normal epidermis.

The smaller the number of recurring nodules the less markedly symmetrical are they and the more they tend to be grouped together in one place, where it is not unusual to find them arranged in circular or semicircular form. We frequently see these groups of papules spreading out at their periphery, while the older lesions in the centre of the group are absorbed; in this manner the disease progresses excentrically, while at the centre the remains of a former eruption (desquamation, pigmentation, or total absence of pigment) will often be plainly noticed.

Not infrequently only a single group of papules, arranged in a circular or semicircular form, is met with; when several are present they may approach each other and thus form various curved figures (serpigines).

The *dry* syphilitic papule does not usually give the patient much discomfort; only during the stage of desquamation an inconsiderable itching may occur. The *moist* papules are much more annoying, as they usually itch and burn, and the resulting fissures and excoriations, especially when near the anus, may become quite painful. Fissures of the hands and feet, in psoriasis syphilitica palmaris et plantaris, may frequently become so painful that the use of these members is thereby greatly curtailed.

In addition to the syphilitic papules, we can often distinguish the initial lesion or its remains. Alopecia, concomitant affections of the mucous membranes of the mouth, nose, pharynx, and larynx, signs of meningeal irritation, affections of the organ of vision, and enlargement of the lymphatic glands are frequent accompaniments of this syphilide; occasionally I have also met with neuralgia, paresis (as a rule of the facial nerve), or some grave symptoms referable to the central nervous system. Affections of the bones, joints, muscles, sheaths of the tendons, synovial sacs, etc., as also gummatous infiltrations not only of the skin but also sometimes of other tissues, are not so very rare as concomitants of the papular syphilide as was formerly supposed.

Diagnosis.

If we bear in mind the description given of the papular syphilide, paying particular attention to the favorite localizations mentioned and to the peculiar form of the eruption according to its seat; if we consider the chronicity of its course; and if we are also able to demonstrate the initial lesion or its remains, and also the involvement of other organs due to syphilis, we shall have the best warrant for a diagnosis of the disease. Nevertheless, as this cutaneous syphilide may easily give rise to mistakes in some of its forms, we must dwell at a somewhat greater length upon the differential signs.

A mistake is most easily made when the syphilitic lesion continues for a longer period in the stage of desquamation and when an unusually great accumulation of scales reminds us of affections whose main characteristic is the formation of scales, as is generally the case in ringworm and especially in *psoriasis*. Such a papular syphilide, which is then also designated *squamous syphilide* (see above) on account of its long stage of desquamation, will the more closely simulate the picture of a tinea circinata or of a psoriasis the more the single lesions take on the shape of discs, rings, and convolutions, which, as we have seen, is frequently the case in a recurrent papular eruption. The differential diagnosis will mainly rest on the following factors.

In *psoriasis vulgaris* the scalp frequently, and also frequently though not always, the extensor surfaces of the extremities are the most seriously affected, and the palmar and plantar surfaces usually escape, and are involved in the disease only when the psoriasis has become general; the redness and infiltration of the skin are always distinctly marked at the seat of the eruption; the white, as a rule silvery mass of scales is broadly lamellated and frequently gathered into high heaps. The upper layers are brittle and readily fall off in

lamellæ, the lowest layer may be peeled off as an adherent membrane, during which process some bleeding of the infiltrated base can hardly be prevented. When psoriasis begins to heal, the skin gradually resumes its normal appearance, and only rarely (in prolonged and intractable cases) does an increased pigmentation denote the original seat of the eruption. When the clinical characteristics are carefully studied, a psoriasis vulgaris may be recognized as such even when, as may exceptionally be the case, it is seated only or mainly on the palm of the hand. In a desquamating papular syphilide, the lesions present an altogether different aspect; here the scales are finely lamellated, not heaped up, and we find a dark brownish base on which they rest and frequently also a dark gray pigmentation. In very rare cases we may find two or three spots of psoriasis on the glans or on the skin of the penis only, the rest of the body being perfectly clean, and such might easily be mistaken for a syphilitic eruption by the novice. The dry smooth surface and the gleaming redness of the eruption will, however, soon convince one that he is dealing with psoriaris vulgaris of the genitals.

Tinea, when situated on the hairy parts, may usually be easily recognized by the unevenly broken hairs, looking as though the part were covered with dust. The similarity of this mycosis to a retreating papular syphilide may be very deceptive when it is situated on a non-hairy part, but a microscopical examination of the scales for mycelia will clear up the diagnosis.

Lichen ruber planus may readily be mistaken for syphilis papulosa miliaris, the more so as the former not infrequently attacks the genitals. We must here bear in mind that the lesion of lichen is composed of small tough, waxy or nacreous, shining nodules with a central depression, which are arranged in groups, at times in bands, often in a circular form; the eruption remains stationary for a long time, and is quite frequently accompanied by intense itching. After recession of the lesion an atrophic spot of a deep dark blue color is left behind, and it not infrequently seems surrounded by a zone of recent lichen nodules, thus forming a picture which presents some similarity to that of serpiginous papules. Desquamation is only slightly marked; the formation of vesicles or pustules is not seen in lichen planus, and ulceration occurs only in consequence of some accidental injury. In exceptional cases lichen planus is also met with on the mucous membranes. The novice is in some danger of mistaking the palmar and plantar syphilide for some other non-syphilitic skin affections; and it will therefore be well to study somewhat more in detail the dermatoses which resemble this luetic eruption.

An *eczema* localized in the palm of the hand is sometimes accom-

panied by the formation of fissures, and it may, when in a condition of desquamation, be easily mistaken for a palmar syphilide; if the intense itching of this affection is remembered, however, and if a few days are allowed to pass, during which time vesicles of the size of millet-seeds filled with a clear fluid are sure to arise, the diagnosis of eczema can be made with certainty.

Lichen ruber of the palm of the hand is rare and may be recognized by the waxy-looking, indented nodules or by the granulations situated on the thickened callous base, and by the intense itching present.

It may be more difficult to differentiate a keratosis of the palmar and plantar surfaces produced by the use of arsenic (*arsenical keratosis*) or a spontaneously occurring callus (*tyloma*) accompanied by the formation of scales and fissures, from a palmar and plantar syphilide; in these cases, as well as in all others which are difficult of diagnosis, we shall have to consider carefully the accompanying symptoms of syphilis (on the genitals, mucous membranes, etc.) which have frequently been mentioned before. We have already spoken of psoriasis vulgaris which affects the volar surfaces.

Not so very rarely a recurrent syphilitic eruption makes its appearance in the form of two or three moist papules, or even only one, on the genitals, in which case it is not easy to distinguish it from the *primary lesion*, which under certain conditions may, as we have already seen, exist in the form of a papule. But the initial papule is as a rule larger than a solitary recurrent papule, and besides there will be present indolent swellings of the neighboring inguinal glands; as, however, the latter may have remained behind from a completely healed initial sore, and as the size of the papule is not conclusive as to its constitutional or primary nature, a further observation of the patient, when the other symptoms which have been repeatedly referred to are absent, would be the only course to pursue.

The differential diagnosis between some papular syphilides and small non-ulcerating gummatous nodules of the skin will be touched on later. In the course of venereal affection, especially in that of a gonorrhœa, we frequently meet with a sort of warty excrescence of the cutis as well as of the mucous membrane, consisting of papilloma-like formations having a more or less slender pedicle, frequently ramifying greatly, or resembling a cock's comb, flattened by pressure, of a bright red color, moist, or drier and covered with a whitish epithelium, ranging from the size of a papilla filiformis to that of the circumference of a finger or even larger.

Although these excrescences are exceptionally caused by a persistent eczema or some other process, it seems to me, in view of the

preponderating frequency of their appearance after long-continued venereal (including occasionally syphilitic) secretions, proper to designate them as *venereal papillomata.* These venereal papillomata cannot possibly be mistaken for moist papules. So long, however, as we continue to call the former "pointed" and the latter "broad condylomata," it will be necessary per longum et latum to mention the points of differential diagnosis of two diseases, which cannot be confounded. Only luxuriating papules (see above), especially when on the genitals or the anus, might be mistaken, on superficial observation, for venereal warts. For the description of these growths the reader is referred to the appropriate section. I may also mention that occasionally both affections are found together in the localities above referred to, and in such cases the venereal papillomata as a rule grow more exuberantly than the syphilitic papules, and the latter may then very readily be overlooked.

The error of mistaking a small *epithelioma contagiosum* (atheroma molluscum, molluscum contagiosum, condyloma subcutaneum) on the thigh, the scrotum, or elsewhere for a syphilitic papule would be more excusable. When carefully examined, however, the first can at once be recognized as a firm nodule, slightly umbilicated and having a shining yellowish color; when pressed between the thumb nails it gives exit to creamy semisolid contents and sometimes also to a crumpled, membrane-like mass.

Before closing our study of the papular syphilide I would draw attention to the fact that after the disappearance of a papular eruption which has continued for some time, pigment spots remain behind, which occasionally, on account of their great number and distinctness, are so striking that we might be tempted to look upon this phase of involution as an independent syphilitic affection, and apply to it the name of pigment syphilide. Indeed, in addition to the pigmentation which remains after syphilitic eruptions, especially of the papular form, some authors insist upon the occurrence of pigmentation as an independent condition not preceded by other lesions.

Leucoderma Syphiliticum.

In very many patients the macular as well as the papular syphilide may disappear without leaving behind any change whatever, but on the other hand, the remarkable fact should be emphasized that in a not inconsiderable number of cases very peculiar pigment anomalies occur after the disappearance of this cutaneous syphilide, and to all appearances they are connected with the antecedent eruption. We observe quite frequently, for example, the development of spots

the size of a lentil to that of a ten-cent piece, where the pigment is diminished in amount or even entirely absent, which spots, as a general rule if not exclusively, are congregated on areas which had previously been rich in pigment. This affection is very appropriately named *leucoderma syphiliticum*. After the retrogression of the first papular or macular syphilide there frequently appear, especially in women, in certain skin areas (which will be touched on later) light colored spots (absence of pigment) of the size of a lentil, which, increasing at their periphery, attain the size of a penny or larger and overlap each other. The margins of the leucodermic spots are as a rule deeply pigmented, which still more prominently emphasizes the absence of pigment. Occasionally the spots of leucoderma are so close to each other that only narrow and frequently concavely notched lines intervene between them. The leucoderma disappears only very slowly, the affected parts being gradually supplied with pigment, which then undergoes its changes within the physiological limits. Six to twelve months are usually necessary for the leucoderma to pass through all these stages; in certain cases even two to four years are necessary. Constitutional treatment does not seem to shorten in the least the course of the disease. During this whole period the affected parts are neither markedly hyperæmic nor does exudation or desquamation take place. The difference in the color of the pigmentation is the only noticeable change in the involved skin area. A. Haslund, however, claims to have seen some spots resembling cicatricial tissue.

According to experience leucoderma attacks preferably individuals with dark complexions. Taylor and other American writers have frequently observed that white spots remained behind after syphilis in the negro; S. Ehrmann also noted a case in a negro, in which the healing of a maculopapular syphilide left behind it white spots.

Varying with habits and customs, with the vocation of the individual and other factors, which influence the deposit of pigment, we may also observe in blond individuals certain portions of the skin which are distinguished regularly by a greater deposit of pigment. And we sometimes see patients of light complexion who are affected in these localities with the leucopathy just described. Field hands and gardeners and other individuals who pursue their vocation in the open air, smiths and bakers, whose skin is exposed to a high degree of heat, present deeper pigmentation on the exposed portion of their skin; in women, again, somewhat more pigment accumulates on the throat, which is left uncovered as a rule, or in the region of the loins, where the clothing makes greater pressure. And in truth

we meet most frequently with leucoderma syphiliticum in the neighborhood of the throat and the loins in women, next on the face, the extremities, and the trunk; occasionally, however, also on the genitals and in their vicinity, which region is usually intensely pigmented. On the whole, leucoderma syphiliticum is found, at least in Vienna, much more frequently in female patients, and usually on the neck; it is possible that some other factors also enter into these considerations.

Leucoderma syphiliticum, as will appear from what has been said, is not to be looked upon as an independent eruption, but as a condition of involution, which not very infrequently follows an antecedent macular or papular syphilide.

It is true that we are not frequently placed in the position to follow the development of this leucopathy from a macule or a papule; mainly for the reason that the involution covers several months at least, and we are only very rarely able to continue our observation for so long a period; and also because the original eruption, when of the macular form, does not show very plainly as a rule on a deeply pigmented skin.

Notwithstanding that leucoderma syphiliticum represents only a stage of involution, the knowledge of its presence is nevertheless very important, because by the localization, size, and arrangement of spots, it is easily differentiated from leucopathies due to other causes, and is therefore of service in enabling us to recognize a previous syphilitic infection.

It would be possible to mistake it only for common leucoderma (*vitiligo*) or for the white cicatrices left behind after scratching excited by *phthiriasis*. In vitiligo, however, light spots are present which are as a rule lighter than those of leucoderma syphiliticum, frequently cover a very large surface, are found in any locality, do not generally present any symmetrical arrangement, and which give the hairs situated within them also an appearance as if devoid of pigment. Besides this there are seen in vitiligo, but never in leucoderma syphiliticum, here and there within the portion devoid of pigment little islets which are more or less deeply pigmented, according as we are dealing with the remains of old or deposits of recent pigment.

When vitiligo and leucoderma syphiliticum coexist, the individual characteristics, as they belong to one or the other affection, may be demonstrated in a very instructive manner.

White cicatrices following excoriations caused by the presence of pediculi vestimentorum are seen most commonly and in greatest number in the region of the neck and loins, and symmetrically distributed as in leucoderma syphiliticum, but the latter exists in the form

of circumscribed round and crescentic smooth spots devoid of pigment, the size of a lentil to that of a cent, while as sequelæ of the scratches caused by the presence of pediculi, we find long radiating, distinctly cicatricial, white streaks.

Pustular Syphilide (Syphilis Pustulosa).

In the same manner that we occasionally observe the gradual passage of a roseolar eruption into a papule, two stages may be observed in the transformation of a papule into a pustule. It cannot be doubted that the pus cocci which are everywhere present, and therefore also adherent to the epidermis, are the cause of this.

As a fact, Roberto Campana and his pupils have repeatedly determined by culture and inoculation experiments that the pustulation of syphilitic eruptions is based on an infection with the staphylococcus pyogenes aureus and albus (Giovanni Botta Burlando). In one case in my ward in the hospital staphylococci were found within the tissues at a great distance from the border of the pustules. The formation of a vesicle at the apex of the papule may be considered as a clinical anterior stage of the pustule. We have, it is true, mentioned in this connection that the contents of this vesicle will be dried up into a scab and fall off, but this does not otherwise modify the retrogression of the papule.

Now it may, however, also happen that one or another papule becomes purulent throughout, and thus forms a pustule; in that case the pustular stage does not as a rule continue long, the upper layer of pus dries up to a scab, and we now obtain an impetiginous eruption, which often lasts several weeks (*syphilis papulopustulosa, papulocrustosa*).

These impetiginous formations are now and then observed together with the papules, and are generally met with on the lower extremities and on the hairy scalp. At first we find present below the raised scab a small ulcer covered with pus; when, however, at the end of some weeks the whole papule has suppurated, the little ulcer begins to heal over, and after the scab has fallen there will be seen a small shallow cicatrix which exactly corresponds to the original papular lesion. On the scalp, while this process is going on, an involvement of the hair follicles which lie within the borders of the eruption may occur, and this will then cause a loosening and falling of the hair. We can then see also, when individual eruptions of the papular syphilide are changed into impetigines, as just described, besides the pigmentation, cicatricial changes in the skin, after the eruption has run its course. In cases in which syphilis attacks individuals

run down in health or when the nutrition of the patient begins first to fail in the course of the syphilitic process, it usually happens that the infiltrate of most of the syphilitic eruptions goes on to suppuration, and that the eruption becomes pustular in this manner. The appearance of the syphilitic pustule is not very different from that of a common pustule, nevertheless there are in the former certain individual peculiarities which are worthy of mention.

The *ordinary pustule* is as a rule distinguished by its acute course, the inflammatory deposit being changed very rapidly into pus, and causing the thin epidermis to bulge and become tense; the latter ruptures very early, and the oozing contents rapidly dry to a scab. The inflammatory halo becomes pale, the scab drops off, and the part is then seen, as a rule, to be covered with recent, normal epithelium. This process quite frequently runs its course in a few days; it is somewhat prolonged only in localities where the circulation is retarded, as in the lower extremities. The peripheral halo is here changed to a circular pustule, and the formation of new epidermis under the central scab does not occur so rapidly.

In the *syphilitic pustule* a slow course is the rule, and is observed even in localities where the circulation is not retarded. The cause of this lies in the fact that the infiltrate is only partially and gradually converted into pus. The epithelial layer covering the pus frequently appears furrowed, and it does not burst so soon because of the low tension, the pustule therefore remaining intact for a long period. But even after the superficial layer of pus has dried to a scab, and this latter has fallen off, the parts beneath are still suppurating, and this continues until the infiltrate in the syphilitic lesion is either absorbed or discharged, which frequently is the work of several weeks. Furthermore, the pustular process is prolonged by the fact that a ring of infiltration makes its appearance at the border of the pustule, and this also suppurates in the course of time, this process being repeated as new annular infiltrations appear. Thus the peculiarity arises that every syphilitic pustule presents an ulcer with slightly infiltrated base and border after the removal of the overlying pustule or the scab. The ulcer involves only the skin or its upper layers, and it increases so long as infiltration of the surrounding parts exists; after the latter has disappeared, the ulcer clears up and heals as a rule, leaving behind a deep, smooth, tender, and at times puffy cicatrix; the latter is particularly noticeable when, after a cleaning off of the ulcer, the granulations rise above the level of the surrounding integument, forming the so-called "ulcus elevatum." The course of the pustule will vary when its fluid contents solidify and combine with the covering of the pustule to form an ad-

herent layer similar to a diphtheritic deposit; the latter after a time breaks down, leaving an ulcer behind.

Should the infiltration and suppuration advance in only one direction while cicatrization progresses from the other side, a semilunar or kidney-shaped ulcer will be formed, whose convex border will be unclean, steep, and infiltrated, thus bearing the mark of progressive disintegration, while its concave border appears clean, flat, and covered with an edge of recent epithelium. In this manner a cicatrix is formed which, following the shifting of the ulcer, assumes a linear form; the ulcer is then called *serpiginous.*

The cicatrices which are left behind thus furnish us with signs, according to their aspect and distribution, which permit our recognition with ease of the nature of the previously existing pustular syphilide.

The locality which the pustule occupies will exert a marked influence on its course. We have already seen that the non-syphilitic pustule, when it occupies the lower extremities, is slower of development and cure; in the syphilitic pustule this condition is expressed in a much more marked manner. When the syphilitic pustules are situated on hairy parts, destruction of the hair follicles takes place and permanent baldness at the site of the cicatrix is the inevitable consequence. Now and then, however, we may observe papilloma-like growths from the base of the ulcer, especially when the pustular syphilide is situated on a hairy part, and glandular, slightly reddened outgrowths covered by scabs or else by epithelium, which as rule again disappear (*frambœsia syphilitica*).

As in the case of other syphilitic affections of the skin, we shall see here also that the pustules of the early period seem to be distributed symmetrically over a large area, while at a later period they occur in single regions only and are grouped symmetrically and in close aggregation. The change of the syphilitic infiltration into pustules is only rarely observed on the palmar and plantar surfaces—more often in children than in adults. Frequently the presence of only one large pustule points to the existence of syphilis. The pustular syphilide, like the erythematous and the papular, makes its appearance soon after infection as the first symptom of constitutional syphilis, as well as a recurring eruption, after the disease has existed for several years.

The pustular syphilide is also usually ushered in with *fever*, but this may occasionally continue for weeks or months, dependent upon the progressive disintegration which is characteristic of efflorescences of long duration.

Together with the pustular syphilide we may also meet, in addi-

tion to the maculæ and papulæ, with all the sorts of syphilitic complications, which we mentioned above when discussing these lesions, and which, like the cutaneous syphilide, are prone to suppuration. Thus in the complicating syphilitic iritis, periostitis, ostitis, adenitis, sarcocele, etc., we are apt to find hypopyon, caries, and other suppurative lesions.

An attempt has been made to divide the pustular syphilide into *impetigo syphilitica* and *ecthyma syphiliticum*, according as the pustular syphilitic eruption is moderate or extensive. I think, however, that we cannot generally draw a sharp distinction, and can therefore accept these terms only with this reservation. We can with somewhat better reason present, in addition to those mentioned, the following forms of the pustular syphilide.

When most of the pustules are umbilicated, thus simulating varicella pustules, there can be no objection to the name, *varicella syphilitica*. Again in those cases in which the infiltration is mainly confined to a follicle, and in which the eruption takes on the appearance of acne pustules, we may speak of an *acne syphilitica*.

Very large pustules up to the size of a half dollar, which develop slowly, arising from flat syphilitic infiltrations, end in *rupia* (from ῥύπος, meaning filth).

No matter in what form the pustular syphilide makes its appearance, weeks, occasionally even months will pass from the development to the involution of this disease; its course may, however, be still further prolonged by the fact that while the older lesions are healing new ones appear, and in this way the course of the affection may be indefinitely prolonged.

Acne and varicella syphilitica are usually found spread over large areas of skin and equally distributed, rupia on the other hand represents a late form of syphilis; it may also, it is true, invade large areas of skin, but more frequently this syphilide is represented by only a few pustules, at times even by a single specimen.

Rupia.

Rupia, which rarely accompanies other forms of eruption, presents such a striking clinical picture that we shall devote an especial description to it. When rupia is present an infiltration of the cutis takes place, which usually involves a large surface but extends only moderately in depth; the infiltration breaks down into pus, a flaccid, round pustule of the size of a cent to that of a half-dollar is formed, the superficial layer of which dries up to a scab.

Under the scab as well as at its periphery a fresh purulent distintegration constantly goes on, whereby a wall is formed around the

pustule, and the central scab, which lies upon newly formed pus, becomes thicker from the drying of the latter.

As its course progresses the annular pustule also dries up to a scab, which is, however, distinctly demarcated from the older and central one, which has in the mean time become thicker. The formation of such a rim to the pustule around the central scab is, as a rule, repeated several times in rupia, concentric rings being thus formed, of which the central ones are thicker and higher, while those more to the outside seem thinner and lower. The accumulation of scabs thus comes to resemble a cone with a flat base, with steps encircling it and leading to its highest point.

The comparison with an oyster shell has been frequently made, as we learn from the designation of the ancients: *pustulæ ostracosæ seu ostraceæ.*

So long as such a rupia crust is surrounded by a reddish ring of infiltration, we may expect that by the transformation of this inflammatory ring into pustules and crusts the lesion will constantly increase in size. The rupia crusts thus often attain the size of a quarter to that of a half-dollar, and after their removal the base of the ulcer is exposed, covered with a thin pus. From the moment that the ring of infiltration becomes pale and is no more changed into a pustular ring, the eruption ceases to spread and goes on to a cure, if no new infiltration makes its appearance at the base. We then observe that the spot in which the disease first occurred, *i.e.*, the central portion, becomes cicatrized, the production of pus here becoming less and less and cicatrization gradually takes place under the crust which has become friable. In this stage we find the centre of the lesion depressed, covered with a cicatrix surrounded by a still raised circle composed of crusts, after whose removal a circle of ulcers more or less deep becomes visible. As healing progresses this ring contracts at the inner side until the whole extent of the eruption is cicatrized.

The cicatrix is about 1 or 2 mm. below the surrounding healthy tissue, and is formed in most cases by a thin membrane which may be thrown up into folds. At an early period, this cicatricial membrane presents a bluish-red tint, but as times goes on it grows paler and paler, until it finally assumes a glistening white color. In exceptional cases only a tough and thick cicatrix is formed, which in time, however, becomes more and more supple.

Should the rupia eruption extend in such a manner that the pustular ring increases in width more towards one side than towards the other, the part affected first, namely the apex of the low cone of crusts, will assume an excentric shape, and the annular ulcer will

necessarily grow chiefly in one direction, until it becomes sickle-shaped, and gradually takes on the properties of a serpiginous ulcer.

The rupia eruption is most frequently observed in an advanced stage of syphilis. Occasionally we find a great many rupia pustules distributed over nearly the whole body, but as a rule this syphilide is limited to a few specimens, and there are cases in which the whole body is free from any recent eruption, and only one single rupia pustule betrays the existence of the constitutional affection. In view of the fact that all the pustules of this eruption do not always appear at the same time, and that the individual rupia lesion occasionally requires months for its development and involution, we may readily conceive that the course of the affection may extend over months, and with improper treatment even years.

Diagnosis.

It will not be difficult from the previous description to diagnose a pustular syphilide, and to distinguish a syphilitic pustule from a non-syphilitic one. In some cases, however, the symptoms are so unusual in their grouping that a few hints on the differential diagnosis become necessary.

Varicella syphilitica, the umbilicated pustules of which are generally located on the trunk and are symmetrically distributed, frequently presents a marked similarity to *varioloid*, so that it may not be easy to say with certainty at a single glance whether we have a mild form of smallpox in hand or the syphilide under discussion. The eruptive fever is probably more intense in smallpox, but we must not lose sight of the possibility of the occurrence of a high fever in varicella syphilitica or a slight one in the initial stage of smallpox. We should therefore particularly remember that in varicella syphilitica it is rare not to find other syphilitic lesions in different localities, which point to syphilis; furthermore that a very long-continued persistence of the syphilitic pustule will be observed in this eruption, frequently lasting for weeks, and finally that the subject of this syphilide is in a very low state of nutrition. When we are dealing with smallpox, on the other hand, a severe case of this disease will, from the activity of the whole process, hardly lead to any mistake, as above mentioned. Mild cases, however, in which only a few pocks are developed, and in which the accompanying fever is of slight intensity, might be the occasion of a mistake. In smallpox, however, the signs of a contemporaneous syphilitic affection will not be met with in other localities, the pustules themselves dry up within a few days, and the whole process runs its course in one or two weeks; further-

more, it is not necessary that a person attacked by varioloid should be in a condition of poor nutrition; the presence of other cases of smallpox in the same neighborhood will also aid us greatly in coming to a proper conclusion.

Acne syphilitica is found in the same locations as *acne vulgaris;* the redness of the lesion is, however, less intense and it is pretty sharply defined from the normal parts; furthermore, its whole course is very slow, and finally the process leads to more extensive ulceration and hence to larger cicatrices. The characteristics already described are therefore sufficient to distinguish this syphilide from acne vulgaris, which besides is very constantly accompanied by comedones, the constant forerunners of the acne nodules.

On the other hand, a mistake could be readily made with *acne frontalis s. varioliformis* (F. Hebra) or with that related, if not perhaps identical form, *acne necrotica* (C. Boeck). We should note that in this form of acne the nodules are found in groups, occupy the forehead and neck as a rule, pass beyond the hair border, and are occasionally present on the face, on the chest, and in other localities. Here the differential diagnosis is so much more difficult for the reason that this acne especially is distinguished by its great intractability, and that it always in healing leaves cicatrices behind, while the developed pustules are transformed into dry scabs, or else a mummification (dry necrosis) of the central part of the nodules takes place very early. It will then be absolutely necessary to look for the presence of accompanying symptoms.

The differential diagnosis between acne syphilitica and *acne cachecticorum* may offer a difficult problem. The true disease, however, can be recognized early if we give proper attention to the accompanying symptoms. Not infrequently we find acne cachecticorum accompanied by caries of the bones and joints, multiple lymphadenitis, and other signs of a depraved constitution. Both affections may, however, present a similar aspect, in so far as the pustules of acne are distributed over the greater part of the body and the extremities, and as most of the efflorescences are transformed into small ulcers; as the patients finally are in a condition of lowered nutrition, they may be attacked by both eruptions under consideration. If we are able to discover in an acne of this kind contemporaneously symptoms of still present or former syphilitic lesions, our judgment of the eruption in a special case will, of course, be a very easy one.

Rupia-like eruptions may doubtless occur during the course of other chronic pustular processes, especially in *pemphigus serpiginosus*. As, however, this latter does not, like rupia syphilitica, run its course with ulceration and maceration of the skin, we have an

important differential symptom in this. After the characteristic crust has fallen off, the ulcer which remains cannot be differentiated from a gummatous one.

In those very rare cases of psoriasis in which the scales are piled up in an atypical manner in the form of cones and concentric layers of scales, and in the cases described by me as *psoriasis ostracea*, the novice might think of rupia syphilitica.

Its localization and distribution, however, as well as the fact that after the removal of the scale, which is frequently of a brownish hue, an ulcer or a cicatrix is never met with, but always a spot covered with epithelium, usually smoothly villous, will enable us to establish the diagnosis of this atypical psoriasis.

Gummata of the Skin and Subcutaneous Cellular Tissue.

The affections of the skin hitherto described present collectively the character of irritative processes; restitutio ad integrum is the usual ending, and even in those cases in which disintegration takes place, as in the pustular syphilide, this is confined to the superficial layers of the skin, unless some accidental complications are added.

The gummatous skin affections run an essentially different course. No matter what may be the final disposition of the gumma, even if it be the most favorable, that of absorption, nearly always the signs of the devastation caused by it will be left behind in the locality where the disease existed.

We see from this short description that the gummatous infiltrations constitute a more serious affection than the irritative forms of syphilis which have been discussed previously. The process is, however, still more serious owing to the fact that it occasionally produces intense pains in the affected parts, which increase at stated periods, frequently in the night, and which are described as tearing, boring, or representing some other quality; sometimes, however, the pains are very slight or are absent altogether, so that patients carry their cutaneous gummata about for a long time, without considering them worth serious consideration or calling for medical attention.

Symptoms.

As regards the gumma and its anatomy the reader is referred to what has been previously said, and we shall discuss here only the clinical course of this specific syphilitic lesion, and distinguish between gummata that have their seat in the skin and such as are located in the subcutaneous cellular tissue, namely between superficial and deep gummatous syphilides of the skin.

The *superficial gumma* of the skin, the *cutaneous gumma* in its narrow sense, occurs in the form of roundish or flat nodules of the size of a pea or larger, which have their seat in the true skin. The lesions consist of sharply defined, usually prominent tumors, at first more or less firm and elastic, but later softer, and of a dull bluish-red color, which is dependent on a chronic hyperæmia. As a rule, the course of the raised gumma of the skin is extremely slow, though occasionally its progress is more or less rapid. The chronic course may be due to the fact that the gummatous infiltrations of the true skin rarely attain any marked thickness. Metabolism within the gummatous nodules is very much retarded, and the central portions, especially of extensive nodules, are more affected by this, so that retrograde processes take place early in their centre. Accordingly necrobiotic processes are only very slowly formed within the small-sized gummatous infiltration of the true skin, which accounts for the persistence of these deposits. We are able on very thin portions of the skin, as on the lids where I have frequently seen gumma, to perceive with especial distinctness that such a gummatous deposit, even though it covers a larger superficial area, does not as a rule pass beyond the thickness of a card, so that we observe a sharply defined, thin, though very consistent deposit, belonging only to the skin, which, apart from the difference produced by its situation, presents a surprising similarity to an initial lesion. Under favorable circumstances its further course is such that the deposit diminishes after persisting for a long time and that the epidermal surface is thrown off in scales, exactly where the nodule was situated; the nodule becomes more flattened and the skin, after absorption has taken place, usually presents a cicatricial (atrophic) thinning and a sharply defined depression over the spot where the gumma was formerly situated. Contemporaneously with the involution the original redness also fades. Because of the very slow course which such a gumma usually takes, hyperæmia leads to a transudation of pigment matter of the blood, which is usually deposited in the form of transformed pigment in the immediate vicinity. Still later the pigmentation also fades, and the spot becomes white and glistening.

If the new deposit breaks down an ulcer is very rapidly formed on account of the superficial location of the gumma. On its surface then the secretion is dried up into a scab, giving rise to a condition which has been very improperly designated a "tuberculo-crustaceous syphilide." When this scab is removed a sharply defined ulcer (*ulcus gummosum*), presenting an unclean base and a sharp, steep border, occasionally undermined, involving various thicknesses of the skin, makes its appearance. So long as the border and the base of

the ulcer remain unclean and infiltrated, it may be expected to enlarge. Only after the infiltration begins to diminish it clears up and a new epithelial covering forms and results in a sharply defined, depressed cicatrix with tender epithelial covering, which is at first surrounded by pigment, and finally becomes glistening white. Exceptionally, however, especially when the ulceration has penetrated deeply and the granulations have been exuberant, the cicatrix is thick and permeated by large vascular loops.

The raised cutaneous gummata rarely occur singly, but as a rule are congregated in groups, and cover more or less extensive areas of the skin. In such a case it is not always easy to distinguish the individual nodules from each other, as the skin presents an evenly red and scaly appearance in its whole extent, by the mingling of the bluish-red and desquamating portions. Only in beginning involution the individual foci become more distinct, and after the healing process has been completed they offer a still greater contrast, for the reason that the depressed cicatrices which have been previously described, taking the place of the gumma nodules, although still closely packed, are separated one from the other by strips of normal integument, the whole presenting an appearance as of a grating.

This formation is very characteristic of the cicatrix of the raised aggregated cutaneous gumma. Occasionally the individual cicatrix is seen to be surrounded by pigment so that the configurations of the cicatrix stand out as from a colored surface.

When, however, gummatous nodules occupying a large area intermingle with each other and go on to suppuration without absorption of the deposit, in consequence of the usual slow course of this process an extensive superficial ulceration will continue for a very long time, and when it finally heals it leaves a large cicatrix behind.

If, however, duplications of the skin, as the external ear, for example, are attacked by these overlapping ulcerating gummata or if there occurs a denudation of superficially situated cartilages (as those of the ears, nose, eyelids, etc.), more rarely of bones, which then become necrosed, the disease will threaten great ravages, the nature of which will be discussed later on.

These destructive processes advance only slowly as a rule, but they may extend widely in the course of a few days. The healing of gummatous ulcerations of the lower extremities is also a very slow process.

When the ulceration persists for a long time in certain localities, as the head and face, papillary growths may occasionally arise from the border or base of the ulcer. This causes the growth of rasp-

berry-like excrescences (*frambœsia syphilitica*), which are surrounded on one side only or altogether by ulcers, the resulting picture being a very peculiar one. The gummatous process of the skin usually appears as a chain of ulcers, with longer or shorter breaks, resulting from the healing of old lesions and the breaking out of fresh ones.

The new gummata either appear irregularly scattered over the surface or the process is confined, perhaps for years, to a narrowly circumscribed portion of the skin. If the latter is the case, the new nodules very frequently surround the original central lesion, which usually heals first in a circular or oval form.

When recent gummata arrange themselves in continually increasing circles around central lesions of older date which have already healed or are in process of healing, we find gummatous rings (serpigines) of considerable size, the different ones being in various phases of absorption and ulceration. When two or more circles meet, the cutaneous affection assumes various semicircular and convoluted forms.

When in the case of a gummatous ulcer of the skin the infiltration is absorbed in one part of the periphery, so that the healing takes place there only, while the process continues at the other border and constantly extends, the new infiltration breaking down again and again, we observe a peculiar ulcerative process, which travels along the surface healing on one side and breaking down on the other—the *serpiginous ulcer*. As a result of the way in which this ulcer is formed its shape must necessarily be that of a kidney or of a sickle, the raised border being on the convex side, corresponding to the successive infiltration and disintegration, while on the concave border or hilus there is an advancing cicatrix.

Occasionally this same process is repeated at different points on the border of the gummatous ulceration, and there are formed a corresponding number of sickle-shaped ulcers, which flank a large cicatrix in such a manner that the borders which are being covered by epithelium face towards the cicatrix. As these reniform ulcers appear much more frequently in the course of syphilis than at any other time, they have been regarded with some reason as quite typical of lues.

There is a remarkable form of gummatous ulcerations, in which an intact islet of skin, left in the midst of the ulcerated surface, is frequently moved from its original position, in consequence of the unequal retraction of the newly formed cicatrix; this is best observed when such a piece of skin which has its seat in the centre of the cicatrix originally belonged to a hairy region, as the eyebrows or the bearded portion of the face, and which seems out of place in the

region where it has been dragged after healing and where it contrasts sharply with parts normally devoid of hair, as the bridge of the nose or the cheek.

The skin affection will deviate from the clinical picture presented so far, when the gummata are not located on the general cutis as isolated lesions, but are distributed more or less diffusely. Extensive areas will then seem tinted a dark bluish-red, the infiltration being at times firm, at others times softer, desquamation going on in some places, superficial ulcerations covered with scabs being found in other parts. These morbid changes, which are usually demarcated by a sharply defined border from the healthy portions, are as a rule characterized by a chronic course, and finally end in the formation of a *syphilitic callosity*, which retracts in time, resulting in distortions (ectropia) of the affected regions.

Calcification seldom occurs in superficial gummata.

While in the superficial gumma we note the development of the smaller infiltrations and see that even the larger ones extend only over the surface, in the *deep* or *subcutaneous gumma* we find the specific morbid product forming nodes of considerable size. It is not very unusual, for example, to find tumors the size of a bean, a walnut, or even the fist, round, oblong, or flattened in shape, which are originally of a firm consistence and readily movable under the skin, or else they appear fixed to the underlying fascia or the skin, according as they originate in one or the other of these tissues. At first the skin covering the gumma, and frequently stretched out over it, generally has a normal aspect; later on, however, various changes are encountered in it.

If the deep-seated gumma grows larger, the skin will gradually become distended, it becomes shining and whiter than in its normal condition; a slight œdematous swelling of the skin may come on later, proving that the gumma is increasing. After it has existed for some time, softening appears at the centre and later also at the periphery. At this stage the examining fingers receive the impression of an elastic, soft, fluctuating mass. Should we be led by this deceptive impression to incise the tumor, no pus will be found as expected, but only a small quantity of a sticky, viscid fluid, not dissimilar to a solution of gum arabic, containing a few pus corpuscles and a drop or two of blood, can be expressed. This phenomenon, as has already been said, gives to these tumors the name of gummy nodules or gummata.

The subsequent course of these tumors is quite variable. If the softened mass of the gumma goes on to fatty degeneration, the newly formed particles of tissue break up more and more into a granular

detritus, and gradually become *absorbed.* It is then found that the skin over the site of the original gumma is depressed and somewhat thinned, but otherwise not materially changed; here and there we note abnormal pigmentation of the part where the gumma was located or of the parts adjacent.

Even should the process have advanced further, so that the skin has assumed a bluish tint and is thinned, and threatens at every moment to rupture, absorption of the deeply situated gumma is still possible. Absorption is then indicated by the fact that the livid color first disappears and gives place to a faint red; gradually the skin pales altogether and only appears still somewhat œdematous; as the gumma declines further the œdema will also disappear, the skin covering the former tumor may even become depressed and then the former seat of the gumma, after absorption is completed, is marked for years to come by a thin (atrophic), pale, depressed area of skin.

If absorption, however, is confined to a part of the gumma, the nodule will also only partly disappear; the portion left behind as a rule then becomes *calcified* or undergoes *cheesy degeneration,* and this acting as an irritant to the neighboring parts and causing inflammation is finally disposed of by suppuration; or else the calcareous and caseous aggregation is enclosed in a newly formed capsule of connective tissue, and remains permanently as a *caput mortuum.*

Another issue which is also observed more frequently in the subcutaneous gummata than in other forms is that of *ulceration.* In this case the softening and breaking down of the gumma extend to the skin which covers it; this assumes a livid discoloration and becomes progressively thinner and thinner until perforation takes place at the highest point of the tumor and gives exit to a thin, purulent secretion and necrosed portions of the gumma. In proportion as disintegration of the gumma and of the skin involved in the process progresses, the ulcer will increase in size. Its borders appear bluish-red, thickened, sharply cut, and undermined; its base is covered by necrotic shreds and is also infiltrated.

The discharge from this is scanty or copious according to the rapidity with which the infiltrate is destroyed. It may also happen that new gummatous infiltrations occur at the periphery during the course of ulceration, whereby the morbid process will be greatly prolonged and the area of the ulcer will be enlarged.

The infiltration of the border and base of the ulcer is diminished by being itself partially absorbed or else is destroyed in part by the ulceration. From the moment that no new infiltration takes place and the old one is totally absorbed or destroyed, the ulcer begins to

clear up; the border becomes flattened, its sharply cut aspect becoming lost, and it gradually assimilates to the base of the ulcer, which latter is then covered with beautiful red granulations in place of necrotic tissue; the secretion also assumes the aspect of "laudable" pus. The more rapidly now the absorption of the infiltrated border progresses, the more rapid is the diminution in size of the ulcer, and finally it becomes gradually covered with new epithelium. An irreparable destruction of the involved skin areas accompanies this process, a cicatrix being always left behind; this scar is rarely smooth but is generally nodulated, and the adjacent parts are often richly pigmented.

The *serpiginous* character of the lesion is more rarely found in the deep-seated than in the superficial gummata, but even here we occasionally observe cicatrization going on in one part while progressive disintegration continues in another.

Although the subcutaneous gumma may usually be easily differentiated from the superficial one, we sometimes meet with cases which must be looked upon as transition forms, or others in which large subcutaneous gummata are associated in such a manner with the superficial ones that the former are surrounded by the latter like a ring, or in which both forms seem to be irregularly distributed in different parts.

Only in very rare cases do we meet with either the superficial or the deep gummata of the skin distributed over the whole body, and even the superficial gummy syphilide, which is almost invariably multiple, is usually confined to a limited extent of surface. The subcutaneous gumma usually occurs singly. It may be found in any part of the body, but occurs with special frequency on the forehead, the neck, over the shoulder blades and the adjacent parts, and on the legs. The smallest gummata are those of the face, as a rule, while those located on the trunk attain the greatest circumference.

The usual slow course of the cutaneous gumma may occasionally, especially in the ulcerative form, become acute, and the destruction caused by the ulceration is often enormous. Persons in poor health, those who have neglected themselves, or who have been subjected to improper treatment frequently have the entire cutaneous surface covered with the ulcers of both forms of gummata. These patients, who are already much debilitated as a result of the extensive disintegration of tissue and the excessive discharges, suffer a further notable loss of vitality in consequence of the fever which accompanies the process. Furthermore, these gummatous ulcerations are frequently accompanied by great pain, which robs the patient of refreshing sleep and which, when the ulcers are localized in places that are sub-

ject to movement, may become altogether unbearable. Even under these circumstances, however, a cure may frequently be obtained.

Most deplorable are those cases in which the gummatous ulcerations are so numerous and are situated so close together that large areas, whole segments of an extremity for example, are so denuded of normal skin that cicatrization is either altogether impossible or proceeds only partially and then with crippling of the joints or other deformity.

If we have to deal, besides, with syphilitic processes which have attacked the fasciæ, muscles, ligaments, periosteum, or bone, and if also destruction of large lymphatic vessels has occurred, we occasionally have an elephantiasic enlargement of the members.

In some cases again the gummatous process begins deep down (in bones, muscles) and finally terminates in ulcerative destruction of the subcutaneous tissue and skin.

But gummata even confined to smaller areas may, when disintegration cannot be arrested, lead to most serious results; thus we sometimes see the tip of the nose or a large portion of the lip destroyed, or necrosis come on from exposure of superficial cartilages, or more rarely of bones, as, for example, the cartilage of the external ear, the bones of the forehead or the occiput, the clavicle, the sternum, etc.; and in addition to the most hideous deformities, there may be grave danger to life. In one of my patients, the coronary artery of the lower lip became eroded during the course of gummatous destruction, and an enormous loss of blood occurred. The dangers are very much greater when the destructive process is very acute, the most horrible destruction sometimes being accomplished in a few days.

Not infrequently, especially when the course of gumma is chronic, the ulcers seated on the remains of the infiltration become covered with epidermis, and we then see the gummata covered with a tender cicatrix of bluish-red tint, which does not always fade in time, as in fully healed cases, but remains hyperæmic as long as any infiltration is present beneath it. We must always be prepared in these cases to see the ulceration which is already healed again break out, should disintegration of these remains of the infiltration set in—a condition which, though of less frequent occurrence in superficial gumma, may still occur in the same manner as we have already described under the heading of the initial manifestation.

When the gummatous infiltration has been wholly eliminated by ulceration or absorption, fresh gummatous deposits are found in the cicatrix only in very exceptional cases, and a new eruption need not be expected under these circumstances. Only in those cases in which

cicatrization covers a large surface, after extensive ulceration, or in which it occurs in locations that are subject to great distention, the cicatrix, like any other, may be insufficient and will then break down even when no new gumma is formed.

Lupoid Infiltration.—When a gummatous infiltration does not progress to total absorption, and traces of it persist for many years without becoming calcified, as we know to be the rule in gummata of the skin, we may sometimes observe a very peculiar change in the morbid process. Small miliary or perhaps larger pale brownish or brownish-red lesions will make their appearance in the persisting infiltration itself and also in the cicatricial and normal surrounding parts, which remind one in every way of lupus, and which also retain their lupous character in their further course. Such lupoid deposits I have repeatedly seen also in connection with other infiltrations of very chronic course and only partial recovery, but most frequently in these "scrofulous" infiltrations, and I am inclined to believe that we were dealing clinically in these cases with a slow transformation of the disease product into *tuberculosis*, and anatomically with a deposit of tubercles in the old infiltration.

Cancerous Transformation.—Another issue of the gummatous process is very rare, but exceedingly grave when it does occur. If a gumma begins to ulcerate and the ulceration drags on for a long period, no matter whether it be due to neglect or to other causes unknown to us, we may fear a transformation of the gummatous ulcer into a carcinoma, as we would in any other long-continued condition of irritation.

Lagneau, Devergie, and Rayer claim to have seen cases in which syphilitic ulcers were transformed into cancer. We are also in possession, as previously mentioned, of reliable observations of carcinoma developing from an initial lesion, or at least appearing on the site of the initial lesion (E. Lang, F. Doutrelepont). Carcinomatous degeneration of gummatous nodules of the tongue has been observed several times (Hutchinson); Langenbeck reported two cases in which a carcinoma of the tongue developed by the side of or on a gumma. I have myself more than once seen the development of cancer on a previously syphilitic soil. Carcinoma in conjunction with syphilis was also observed on the cheek and the hard palate by F. Doutrelepont.

Esmarch distinctly claims as regards rodent ulcer that in some cases it is nothing else than a form of inveterate lues.

We must not overlook the fact, however, that carcinoma may also make its appearance in patients who chance to be suffering from syphilis. I had an opportunity, at my clinic in 1883, to watch the

development of a carcinoma from a gummy ulcer and to study it most carefully.

Stage of Syphilis at which Cutaneous Gumma Appears.—It is probable that gummata of the skin, like gummata in general, make their appearance usually during the later stages of lues, although they may in some cases be developed during the existence of a primary syphilide of an irritating character; individual syphilologists, however, venture too far when they maintain that gummata do not occur with moist papules (mucous patches) in the same individual, and therefore feel justified in distinguishing the "papular" stage sharply from the "gummatous." I have seen very characteristic gummata develop after the first roseola eruption; gummata occurring with moist papules may also be observed, whether the latter have preceded the advent of the gummata or have followed it. Hereditary syphilis, moreover, frequently permits the observance of this coincidence. It is true, however, as a general rule that gumma rarely develops within the first few months after infection; it is somewhat more frequently seen after the first half-year. It is most commonly observed during the first five years of a syphilis, and after this time cutaneous gumma probably occurs much less frequently; we are, however, in possession of sufficient observations by myself and others, in which cutaneous gummata (as well as gummata in general) appeared twenty, thirty, forty, and even fifty years after infection. In accord with this, we only rarely observe recent irritative symptoms of syphilis with cutaneous gumma, but more likely the pigmentations and cicatrices left behind by the former; in the same manner the traces of a chancre are at times plainly to be seen. It is not unusual to find the simultaneous presence of gummatous deposits in the bones and in the oral, nasal, pharyngeal, or laryngeal cavities, a syphilitic affection of the intestines, of the nervous system, etc., or cicatrices, healed perforations and defects, long-standing paralysis, etc., after more or less grave syphilitic processes have run their course. Numerous lymphadenitides are probably also frequently found; they should, however, be looked upon either as diseases by themselves, or as survivals from the irritative stage; lymphatic glands which have remained healthy up to this time very rarely become enlarged from gummatous infiltrations of the periphery; on the other hand, one or another of the lymphatic glands frequently becomes painfully enlarged in cases of relapse. The gummata of the lymphatic glands will be considered below.

Although gumma of the skin may of itself constitute a very grave affection, the greatest danger is that the process may involve later one or another of the vital organs. Nevertheless very favorable re-

sults are frequently to be obtained, although accompanied here and there by disfiguring cicatrices, annoying defects, or other permanent disturbances.

Diagnosis.

Although a recognition of the gummatous skin syphilide is not attended with any great difficulty according to the description given above, we must nevertheless admit that a gumma may occasionally be easily mistaken for some other affection, and the differential diagnosis of cutaneous gummata from other syphilitic affections of the skin is not always easy.

Let us consider first the gumma of the skin which occurs in small lesions, the superficial gumma. It may at times be difficult to differentiate the bluish-red, scaling, sharply defined superficial gumma, the size of a lentil, when it is still intact, from some *papular syphilides;* we should then recall that although an even symmetrical distribution is common to papules, these may, however, when they appear as recurrent lesions be massed into groups just as irregularly and arranged in curved figures as frequently as the raised gumma nodes. Individual efflorescences of the papular syphilide, which are located in moist and macerated parts, assume, it is true, the characteristic appearance of the mucous patch, but in the absence of such a localization of the affection as well as of many other of the attendant symptoms, it may be difficult to decide at once whether the pathological product should be classified as an early or a late symptom of syphilis. Even in this case, however, further observation will establish the diagnosis in all certainty. The papules, unless the patient is very greatly debilitated, very rarely ulcerate, and will heal, leaving behind only pigmentations, possibly also slight cicatrices; gumma of the skin, on the other hand, not infrequently breaks down even in the well-nourished, and will leave behind a depressed cicatrix or parts changed by cicatricial tissue, even when ulceration has not occurred.

The knowledge whether a present ulceration is the result of a gumma, a pustule, a papule, or indeed of an initial lesion, is also of great importance. Ulcerating papules and *pustular syphilides*, especially acne syphilitica and varicella syphilitica, belong to an early stage, are as a rule observed in badly nourished individuals, and are generally distributed over the body in large numbers. The ulcerations arising from gummata also occur in well-nourished patients, and are frequently met singly. The size of an ulcer arising from a papule is, as a rule, determined by the circumference of the papule; the ulcer left behind by a pustule is frequently enough seen

to increase at the periphery in such a manner that the infiltrated, reddened, sharply cut border, which looks here and there as though it had been bitten into, also goes on to disintegration and raises a pustular wall, which precedes the further peripheral extension of the ulcer. In cases in which only isolated syphilitic pustules are present the ulcers may be recognized as arising from these by the fact that they rarely increase in depth but frequently enough in surface area, and this always occurs after the previous formation of a pustular ridge. If the ulcer is seen at a time when the formation of pustules has ceased, its differentiation from a superficial gummatous ulcer is difficult and frequently impossible.

An ulcer which has its seat on an initial lesion is deep only in the centre and grows more superficial towards the edge; but even when the edges of the ulcer are steep, the characteristic sclerosis of the base and of the periphery and the complicating affections of the neighboring lymphatic glands, which are rarely absent, will prove to be valuable diagnostic points. The chancrous ulcer is usually single, while gummatous ulcers are frequently multiple; their edges are infiltrated, sharply cut, occasionally undermined, bluish-red, but not very firm, and at times the ulcers assume a serpiginous character. When swelling of the lymphatic glands of the neighborhood is present, investigation will usually reveal the fact that it was present before the ulceration occurred, for adenopathy is seldom an accompaniment of gumma. It goes without saying that the accompanying symptoms are also to be taken into consideration in forming a diagnosis.

Among the non-syphilitic morbid processes, *scrofulous* infiltrations and ulcerations of the skin (scrofuloderma) are deserving of our first study. They may, like gummy ulcers, occur as either single or multiple lesions, and they also generally persist for a long time. Here the observation of the following factors will often help us in avoiding mistakes. Subcutaneous scrofulous infiltrations, even when they are originally rather firm to the touch, soften very early, and as a rule lead to very great thinning of the overlying cutis, so that, when purulent disintegration takes place, the skin becomes perforated at one or more points, giving exit to thin pus. Examination with a probe will show that the thin integument is non-adherent to the underlying tissues over a large extent of surface. Even in those cases in which several openings join each other, and large, round, or longitudinal apertures result, we shall find the skin undermined, thinned, and floating over a large area. If the process goes on of its own accord to recovery, adhesions between the thinned skin and the underlying tissues will be observed only in the rarest cases. The edges of the

skin are rather frequently rolled inwards, and present a surface covered with an epithelial layer to the base of the ulcer as a result of which the cicatrix will naturally be covered or surrounded by cushions of various shapes. If the discharge of pus takes place in a manner that the skin remains intact over the scrofulous ulcer in the form of a bridge, a so-called bridge scar (*Brückennarbe*) is formed, after the free edges of the bridge have rolled inwards and the base of the ulcer has been covered independently with new epithelium, under which the probe can be passed freely. Should a triangular flap of skin project over the surface of a scrofulous ulcer, and its edges roll in so as to prevent adhesion of the flap to the base of the ulcer, upon healing of the latter a pointed cicatrix will remain. In a similar way various other curiously shaped scars may be formed. The characteristic enlargement of the lymphatic glands as well as other signs of a torpid or asthenic scrofulosis will furnish us besides with sufficient differential points to permit a recognition of the scrofulous nature of the ulcer and its cicatrix as such.

The resemblance of a cutaneous gumma to *lupus* may in some cases strike one as being even more close than that to a scrofulous infiltration. We find large, dark blue, bluish and brownish-red nodules of various sizes, which in part break down, in part mark the skin with cicatricial tissue, just as does lupus in the absence of ulceration. The fact that the process selects the face by preference, causing defects and disfiguring cicatrices, and the further fact that a chronic course is characteristic of both processes, render it extremely difficult for the novice to make a correct diagnosis. The difficulties of diagnosis may in a few cases increase in such a manner that even experienced physicians have had recourse to the expedient, which at all events must be viewed as a sign of their embarrassment, of employing the term "lupus syphiliticus" in these doubtful cases; but in this they do an injustice both to lupus and to syphilis.

In cases in which unusual difficulty exists in the differential diagnosis, it is advisable to wait for further development before reaching a positive conclusion. The cases in which the difficulty will not soon disappear are very few indeed. The following points will generally suffice for a positive differentiation between lupus and syphilis: The lupous process, as a rule, commences in earliest childhood (rarely at the age of puberty and more infrequently still in advanced life), runs almost without exception an extremely slow course, and in the overwhelming number of cases is symmetrically localized on the face. The infiltrations occur in lupus as a rule only in very small foci, which are more readily discovered by sight than by the touch. Although at times lesions the size of a nut or even larger are found,

these never reach the circumference of large subcutaneous gummata; they are also with few exceptions soft from the beginning, and nearly always break down. After lupus has healed over, disfiguring contractile and generally bulky cicatrices are left behind. We therefore quite frequently miss the sharp delimitation from the healthy tissues surrounding the infiltrations and cicatrices of lupus.

Quite frequently the lupous infiltration recurs while healing is progressing, so that even cicatrized portions may be again attacked by lupus; we consequently often see in a case of lupus, infiltration here and disintegration there, here cicatrization and there fresh infiltration of the cicatricial tissue.

A spontaneous cure of lupus is possible, it is true, but is of rare occurrence; rather this disease, especially when left to itself, continues during the whole life of the patient. A sudden change of the slow process of destruction into a rapid one is rarely observed in lupus, usually only when it becomes complicated with carcinoma; Hebra, Kaposi, Volkmann, F. Doutrelepont, myself, and others have observed cases of this kind. Lupus in the majority of cases commences on the skin; mucous membranes immediately adjoining or near the skin are as a rule involved in the morbid process only secondarily, although lupus originating in the mucous membrane may be met with. In rare cases the lupous process continues to advance, involving finally even the muscles, bones, and cartilages, but as a rule only when these structures are near the skin; this, however, occurs only after the disease has existed for years.

The course pursued is altogether different in gumma of the skin; this usually makes its appearance, as it must be looked upon as the expression of a syphilitic affection which has already existed for some time, at a later age than lupus. The sharply defined infiltrations are as a rule united to form extensive lesions; the cicatrices, in part thin and smooth, in part bulky, are also sharply circumscribed; healed portions after complete absorption or ulceration of the infiltrate are not generally, as in lupus, affected again; it is only after the infiltration has existed for a very long period that we may occasionally see tuberculous or lupoid disease invading the site of a former gumma.

The course of the syphilitic process, although very slow as a rule, is far more rapid than that of lupus, and consequently the loss of tissue appears earlier in this disease than in lupus. If we add, also, that this syphilide attacks the skin in the majority of cases asymmetrically, that together with it there are also present other symptoms of past or still florid forms of syphilis, and that lastly the affection under consideration will promptly improve under antisyphilitic treat-

ment, we have pointed out the most important aids to a differentiation of this disease from lupus.

It may also be pointed out, as lupus most frequently attacks the skin of the face, especially that of the nose, that a gumma (which is not infrequently also found in this neighborhood) usually produces a perforation of the bony septum of the nose, even destruction of this bone and of a portion of the cribriform plate of the ethmoid, and as a result we find a saddle-like sinking in of the bridge of the nose, which is not the case in lupus. It is said that, as a general rule, the perforations caused by lupus involve only the cartilaginous septum, while syphilitic perforations attack the bony septum. I cannot accept this statement, however, for I have quite frequently seen a destruction of the cartilaginous septum alone in the course of syphilis.

If we will always bear in mind the differential points just detailed, we shall have little difficulty in distinguishing between lupus and a syphilis acquired in childhood or even hereditary syphilis; in the latter case, furthermore, a symmetrical localization of the gummatous deposits is the rule. Hutchinson has pointed out as signs of hereditary syphilis, other characteristic changes in the teeth, the eyes, etc.; these are valuable aids in the diagnosis, yet we must remember that they are not very rarely observed in the absence of syphilis. In passing, I must point out that patients suffering with lupus may also acquire syphilis; in this complication, which I have observed several times, both morbid processes are of course distinctly observed side by side.

The picture becomes still more complicated when an individual who has been suffering previously from various other forms of chronic skin disease contracts syphilis. Thus, I found, in the case of a debilitated man who had been suffering for years with scrofula and who had acquired syphilis, syphilitic papules side by side with tuberculosis verrucosa cutis and scrofuloderma.

In comparison with lupus, a chronic tuberculosis of the skin (and mucous membranes), *acute miliary tuberculosis* of the skin is very rare, nevertheless it will be well to describe briefly the characteristic symptoms of this disease, for the reason that it may be readily mistaken for lues by the inexperienced. Miliary tuberculosis of the skin as a rule is an acute process which rapidly leads to disintegration; we are therefore hardly ever in a position to study its early stages, and are usually confronted with a fully formed ulcerative process. The ulcer is flat, the base of a pale red or yellowish color, its border is as though nibbled, and occasionally presents whitish miliary nodules which when they fall off leave behind them cavities of the same size as themselves. The surrounding skin is not markedly reddened, and

pronounced infiltration is usually absent. The secretion and especially the nodules contain tubercle bacilli, although we are not always able to demonstrate them. The pain of the tuberculous ulcer is sometimes excessive. The general condition of the patient is usually poor, for the reason that tuberculosis of the lungs is very frequently also present, to which the patient rapidly succumbs. When the course of the disease is somewhat milder, cicatrization of the centre of the ulcer may possibly take place; the tuberculous process, however, progresses constantly at the periphery.

Another fact which it is important to bear in mind is that tuberculosis of the skin may also occur under a different clinical picture. Occasionally the tuberculous process begins as an infiltration of the subcutis, and only later reaches the surface, appearing here as a fungoid mass, or going on to ulceration; in such a case there is no formation of nodules (*tuberculosis fungosa*). At another time tuberculosis of the skin assumes the form of (single or multiple) ulcers the character of which is revealed only on microscopical examination.

The differentiation of a gummy syphilide of the skin from *lupus erythematodes* is not a matter of any difficulty to the experienced physician, but a novice might be more or less perplexed, mistaking perhaps a lupus erythematosus for a syphilide, on account of the sharply outlined, frequently round or ring-like infiltrations, the involution of which frequently leads to cicatricial changes in the skin.

The more vivid red of lupus erythematosus, the presence of a small crust which appears fatty to the touch, and from the under surface of which a thin cylinder is seen to extend to the mouth of a sebaceous gland, the generally superficial seat of the infiltration, and the nearly regular absence of ulceration in this disease, together with an absence of other syphilitic symptoms, all furnish important data for the diagnosis.

We are quite frequently placed in the difficult position of deciding between a gumma of the skin and a *superficial cancer* (rodent ulcer). The question will in truth become one of considerable difficulty when apart from the gumma no other symptom of syphilis is present, when there is a history of the affection having existed for a number of years, and when the destruction of the parts attacked is of such a character as to suggest the ravages of a rodent ulcer. The following will serve as differential points: The superficial carcinoma, as a rule, commences in the form of a parchment-like change in the skin and the latter is found, at the spot thus changed, of a yellowish or pale brown color, depressed, and surrounded by a firm rim, a line in thickness, raised above the surface. This rim will either present the same color as the part it surrounds, or it is reddish if the vessels

coursing through it are dilated. Not at all infrequently the beginning skin carcinoma is hidden by the picture of a seborrhœa. The epithelial layers are usually at first very intimately connected with each other, so that no desquamation occurs for a long time, but when the epithelium once becomes loosened, denudation of the succulent lower cell layer takes place at the same time, and this layer is then only in the rarest cases covered with a permanent horny layer of epithelium. In this manner the first loss of substance takes place, and the denuded surface secretes a scanty, thin, sticky fluid, which dries up into an ephemeral membrane or a thin yellow crust. This spot is doomed to destruction, and a small ulcer makes its appearance, the base of which in most cases is of a beautiful bright red color, shining, and looking like a granulating surface; it is, however, rough to the touch, and is always surrounded by a somewhat firm border or by a nodular wall, which generally increases in size as time goes on. As the carcinomatous ulceration progresses epithelial plugs are frequently pressed out. Occasionally the carcinomatous elements grow exuberantly and do not ulcerate away with equal rapidity, so that the base of the ulcer becomes level with the surface of the skin, and may even rise above it, and we then have the *ulcus elevatum*, which is firm to the touch and of a bright red color.

Although the course and the growth of the superficial carcinoma are exceedingly slow, the phenomena attending a loss of substance are nevertheless observed quite early, the skin being more and more drawn towards the carcinoma, radiating folds seeming to pass from it in all directions. This drawing of the skin towards the advancing carcinoma is the cause of the frequent distortion of the angle of the mouth, the lips, alæ nasi, eyelids, or other parts. In time carcinomatous infiltrations of the neighboring lymphatic glands will follow.

If we therefore take into consideration the fact that the gumma when superficially situated results in the formation of a smooth scar, and even when a thick radiating cicatrix is left, as in the deeper gummatous ulcerations, it will occasion marked distortion only when the loss of tissue is very great, we shall, taking into consideration also the other possible symptoms of syphilis, only very rarely mistake this for a carcinoma. At the same time we should not forget that both affections may accidentally exist side by side, and also that transformation of gummata into carcinomata has been observed.

The possibility of mistaking *atheroma*, *multiple lipoma*, *neuroma*, *cysticercus cellulosæ*, *sarcoma*, or *actinomycosis* for gummata of the skin, need only be mentioned, and we may also observe here that rare cases have been recorded in which *glanders* and *leprosy* were confounded with syphilis. It cannot be denied, however, that many

other forms of disease, which are ordinarily easily recognized, may occasionally be so greatly changed under certain circumstances that doubt may arise as to their nature. One of slight experience is then involuntarily reminded of the well-known adage, "in dubiis suspice luem." We cannot in an article of these limits enter into a detailed description of all possible cases of this sort, and the requisite knowledge and skill can be acquired only as a result of long clinical experience. We shall do well, however, to refer a little more particularly to two instances in which error might arise.

Rhinoscleroma will usually be easily recognized by its rigid, sharply defined, deforming infiltrations which, starting from the nose, invade the skin (upper lip, cheek, etc.) as well as the mucous membrane (gum, pharynx, larynx) in the immediate vicinity, rarely also the bones (in one case I observed the scleroma filling up both orbits), only exceptionally leading, if left untreated, to an extensive loss of substance, but sometimes after years to a destructive scar-like atrophy. If other disturbances, however, complicate the morbid process, as for example repeated but yet insufficient cauterizations, a loss of substance may occur in the strongly infiltrated nostril, which might easily lead us into an error at first sight.

Conversely also a gummatous infiltration of the nostril may resemble a rhinoscleroma, but fortunately the result of a proper antisyphilitic treatment will very soon enable us to make a correct diagnosis.

Ringworm (tinea circinata), as we have already mentioned, may at times simulate closely a cutaneous syphilide; but the danger that one of small experience may mistake a tinea sycosis for a syphilitic trouble, especially for a gumma, is much greater. A mistake of this kind is, however, readily avoided. Parasitic sycosis is usually observed on the face, and also on the head (in the latter case it is called *kerion Celsi*) and occurs in the form of sharply circumscribed doughy tumors, the size of a pea to that of a half-dollar, a few millimetres to a centimetre in height, from which protrude here and there broken hairs which are easily pulled out. After the hairs fall out or after they are removed, openings the size of the point of a needle remain behind, from which pus quite frequently oozes in drops on pressure. In the hairs the characteristic fungus elements of the trychophyton may be demonstrated, provided the suppuration has not destroyed the fungus, as is not infrequently the case. Occasionally we may find plainly developed patches and rings of tinea tonsurans on other portions of the body.

Other affections may accidentally assume a more or less striking resemblance to syphilis. Thus I once saw an ulcerative process of

the nose, which suggested syphilis at first sight. On careful examination, however, it soon developed that the bluish-red tint and the doughy soft œdema of the inflamed part were due to a *pernio*, which had led to an ulcerative process as the result of improper medication, the parts around being in a condition of inflammatory irritation and giving exit to an excessive secretion of sebaceous matter; some of the individual ulcers were studded at their base and on their edges with small papillary growths, suggesting not only syphilis but also carcinoma. A moderate antiphlogistic treatment resulted in a cure.

Mastitis Syphilitica Simplex et Gummosa.

Inasmuch as the mammary gland lies in or below the panniculus adiposus, and diseases of it, which may be met with during the course of syphilis in the male as well as in the female, may be most easily recognized upon an examination of the skin and the subcutaneous tissue, it will be well to discuss syphilitic affections of the breast in this place.

Most writers of text-books appear to be satisfied when they have mentioned the syphilitic initial lesion or papules occurring on the nipple, which have already been touched upon by me, and do not even allude to the other affections of the true mammary gland, or else they specifically deny the occurrence of syphilitic lesions of the mammæ, other than chancres and mucous patches of the nipple; and this notwithstanding the publication by Ambrosali in 1864 of three cases (in two girls and one man) of enlargement of the mammary glands cured by the administration of potassium iodide. There is no reason whatever to doubt that the mammary gland may become diseased as a result of syphilis; and Lancereaux has recently called our attention again to syphilis of this part.

We find the mammary gland occupied by a diffuse or circumscribed, frequently irregularly outlined, occasionally sensitive infiltration, which may also involve the skin. When the gumma breaks down and discharges, the skin after cicatrization becomes adherent to the deeper structures. Occasionally only the area of the nipple seems to be involved. Mastitis syphilitica interstitialis et gummosa is, however, rare. Interstitial mastitis may be observed in the first stages of lues, but more frequently it, as well as the gummatous form, is met with during the later stages of the disease.

The syphilitic disease of the mammary gland, which is at all events rare, may have been at times overlooked, or again have been mistaken for a carcinoma.

During recent years our attention has been attracted to tubercu-

losis of the mamma. As this affection usually arises in the skin and only later invades the glands, we must keep in mind the characteristics of the previously described tuberculous ulcerations, to avoid mistaking it for syphilis of the mammary glands.

Syphilis of the Hair and Nails.

In the course of syphilis various diseases of the *hairs* are met with, which are either symptomatic of the general disturbance of nutrition, or are the expression of a local morbid process.

In a very early stage of syphilis, soon after the appearance of the first constitutional symptoms, and also in later stages, we frequently observe that the hairs become dry and lustreless, and are loosened in their roots, on account of which they fall out (*defluvium capillorum*) either in small but numerous areas or over the whole scalp, occasionally only in such a manner that the hair seems to be distributed in bundles over the head. In rare cases the thinning of the hair increases to total baldness (*alopecia*), which as a rule occurs only on the head, but now and then may involve also the eyebrows, eyelashes, axillæ, pubes—in short, all the hairy parts. This form of alopecia, which is generally accompanied by some cutaneous syphilide, may frequently outlast the latter and continue as a symptom by itself; with this there is, as a rule, no strikingly diseased condition to be observed on the hairy scalp, especially no desquamation, no reddening, and no inflammation. In most cases the defluvium will cease at last after weeks or months and new hair will appear, but it does not always reach its former luxuriant growth; it is only in rare instances, however, that the baldness becomes permanent. It is not improbable that trophoneurotic disturbances, whether of syphilotoxic or other nature, are factors in this alopecia.

Besides this alopecia we meet in syphilis with another form which is accompanied by desquamation and so-called seborrhœa sicca, in which, however, it is difficult to detect any characteristic symptoms of lues.

That form of alopecia which accompanies syphilitic eruptions on the hairy parts, especially on the head, occurring in the form of maculæ, papulæ, and gummata, has already been alluded to in its proper place; and I wish again to emphasize the fact that those syphilitic processes which lead to the destruction of the soil infiltrated by them produce an irreparable loss of hair; this is of very frequent occurrence after gummatous and pustular ulcerations, but is more rare after papular lesions.

Affections of the *nails* which are manifested by dulness, discolora-

tion, irregular deformities, splitting, and splintering, only rarely occur by themselves; they usually accompany a palmar or plantar syphilis, which extends as far as the fingers or the toes, or which is especially located on the digits, and persists unchanged for some time after the palmar and plantar syphilide has disappeared. In these cases the diseased nails only very gradually return to a normal condition, and indeed they may never be entirely healed.

When the bed of the nail is the seat of a syphilitic deposit, a papule or a gumma, we speak of an *onychia syphilitica;* this is accompanied by redness and swelling of a more or less extensive portion of the ungual phalanx, and the nail also will be more or less discolored, corresponding to the greater or less amount of infiltration. On account of the enormous resistance of unyielding tissue, the process is exceedingly painful.

When the syphilitic deposit is localized on the matrix or the lateral nail furrow, the affection is called *paronychia syphilitica.* This may, according to the nature of the process, be caused by an initial lesion, a papule, a pustule, or a gumma developing in the course of a constitutional syphilis.

The initial lesion as well as the constitutional papule and pustule are very apt to suppurate when situated on the nail furrow; ulceration of a gumma occurs still more frequently in this locality. In the latter case, the nail is thickened, infiltrated, and presents an ulcerating edge towards the nail-furrow. Paronychia syphilitica is also accompanied, provided some part of the pathological process occurs on the bed of the nail, by violent pain, which persists until absorption of the deposit or healing of the ulcer occurs. Affections of the nails occur for the most part on single fingers or toes, but I have frequently observed their occurrence on several at the same time. When the matrix and the bed of the nail are also affected, the nail or part of it will be lost, and it is in any case only rarely reformed in its normal shape.

SYPHILITIC AFFECTIONS OF THE DIGESTIVE ORGANS.

Syphilis in all its stages shows a special predilection for the beginning of the digestive tract, the lips, and the oral and pharyngeal cavities, these parts rivalling the general integument in this respect. The full knowledge of the pathological processes which occur here is therefore of the greatest importance for a correct interpretation of the local changes as well as of the general affection. The remaining portions of the digestive tract are perhaps not so frequently the seat

of gummatous deposits, syphilitic callosities, and possibly also irritative conditions; the diagnosis of these conditions is, however, much more difficult, especially that of the irritative troubles, which are generally of a simpler nature and produce at the most only temporary disturbances, and may only occasionally be suspected when affecting the inaccessible portions of the digestive tract.

The Oropharyngeal Cavity.

Initial Lesions.

In consequence of the manifold opportunities which exist in these parts for syphilitic infection we quite frequently meet with the initial lesion on the *lips*, the *tongue*, etc. The infection is communicated either directly by kissing, sucking, etc., or indirectly by eating- and drinking-vessels, pipestems, instruments, and other objects which have been used by syphilitic persons. Thus Spillmann tells of a thirteen-year-old paperhanger's apprentice, who had an indurated red spot on the lower lip, which was a chancre acquired from a man suffering with syphilis of the mouth, with whom he worked, picking the nails from the same bag; paperhangers have the habit of holding a quantity of nails between their lips, and returning those not used to the bag. In all probability the apprentice was infected by virus adhering to one of those nails which had been held by the man between the lips.

I have repeatedly observed the initial lesion in males as well as in females on the *gum* of the upper jaw (externally and facing the hard palate), as a characteristic ulcerated infiltration accompanied by scleradenitis of the lower jaw and constitutional symptoms. A characteristic chancre on the hard palate was observed by me once in the case of a virgo intacta. The *tonsils*, according to my experience, are quite frequently the seat of syphilitic initial lesions. L. v. Schrötter also mentions an initial lesion on the posterior surface of the velum and on the Eustachian tubercle; the infection had been communicated by a Eustachian catheter.

The work of L. Duncan Bulkley, of New York, to which was awarded the Alvarenga prize of the Philadelphia College of Physicians—"Syphilis in the Innocent" (syphilis insontium), New York, 1894—is replete with details of a most interesting character, relating to cases of this sort.

The initial lesion makes its appearance at the beginning of the digestive tract, as it does also in other localities, either in the form of a more or less distinctly marked chancre, which under certain circumstances may become eroded or ulcerated, or in that of a pap-

ule, which passes through the transformations natural to it. The *period of incubation* is the same as in other parts of the body, and enlargement of one or more lymphatic glands of the immediate neighborhood also occurs, here as elsewhere, as a constant attendant of the initial lesion. The recognition of a chancre or of a papule in the upper portion of the digestive tract as an initial lesion is therefore easy, if we take into consideration the duration of incubation and the gradual development of the initial lesion as well as the accompanying indolent lymphadenitis, and finally also the outbreak later of a constitutional syphilis which occurs in the majority of cases. Constitutional symptoms are perhaps met with just as frequently during the course of syphilis in the first portions of the digestive tract as in that of the skin; the irritative initial forms are naturally also more prominent than the later symptoms of the affection.

Erythema.

Among the mildest of the irritative forms we may mention simple hyperæmia, erythema, which appears on the but slightly infiltrated mucosa in patches from the size of a lentil to that of a penny. Quite frequently these areas of hyperæmia are sharply defined and distinctly raised above the healthy portion.

The erythemata of the size of a lentil to that of a penny usually are found on the mucous membranes of the lips or the cheeks or at times on the dorsum of the tongue, while those extending over a larger surface occur chiefly on the soft palate and also spread further to the faucial tonsils, the uvula, and the posterior wall of the pharynx. When the latter is the case, a picture similar to that of a catarrhal angina is presented, only the erythema of the mucous membrane of the palate and pharynx which is due to syphilis, and which might also with propriety be called *angina syphilitica erythematosa*, is not as a rule accompanied with any intense swelling, and furthermore the area of redness, especially when seated on the soft palate, is sharply defined anteriorly. This erythema of the mucous membrane, which may be compared to the erythematous skin syphilide, makes its appearance most frequently as an accompanying symptom of a primary syphilitic eruption of the general integument, either together with the cutaneous syphilide, or a few days prior to its appearance; not infrequently it represents the first perceptible sign of the constitutional affection, which is then followed by others.

Erythema of the mucous membrane alone is also occasionally ushered in by fever; in the exceedingly numerous cases in which angina syphilitica erythematosa makes its appearance together with the

first symptoms of a generalization of the syphilitic infection, it is evident that the fever of invasion will as a rule precede its appearance.

The annoyance to which a patient is subjected in consequence of the erythema of the mucous membrane is very slight in the beginning; at first the sensation of dryness in the diseased parts is most noticeable, next that of the extraordinarily large formation of mucus. Only rarely does the angina retrograde in a few days, but as a rule it lasts for weeks, and spreads over the whole velum, the uvula, the palatine arches, the tonsils, and the pharynx. In the further course of this affection the epithelium is thrown off as far as the papillary layer, and sharply defined erosions covered with a red or a whitish deposit make their appearance, surrounded by narrower zones of infiltration. An infiltration which is at all large will cause the palate and the pharyngeal wall to become rigid. The movements occurring with deglutition and speaking become laborious, and may even lead to slight lacerations of the mucous membrane (fissures), especially at the point where the anterior arch of the palate is joined to the tongue, and on other exposed localities, which now become extremely sensitive to the slightest irritation. After the infiltration has existed a number of weeks it declines, the erosions and fissures become covered with epithelium, the bluish-red mucous membrane takes on a rusty brown color and appears permeated by loops of blood-vessels, which condition lasts for some time after healing has taken place.

Resolution of the erythema of the mucous membrane either takes place at the same time with the involution of a contemporaneous cutaneous syphilide, or the affection of the mucous membrane runs its course independently of the condition of the skin.

The frequent *recurrence* of angina syphilitica is very characteristic; recurrences will make their appearance during the first year of infection and sometimes later still, either alone or with others in different localities.

Enlargement of the lymphatic glands of the neck is rarely absent in association with erythema of the mucous membrane.

In the same manner that we occasionally observe on the skin the gradual transformation of a roseolar eruption into a papular one, so we also notice that occasionally some portions of the erythema of the mucous membrane are transformed into papules, which on account of their situation on the mucous membrane present many points of difference from those on the general integument.

Papules.

The syphilitic papule of the mucous membrane presents a flat red elevation of the circumference of a lentil or over; it is sharply defined and is in its early stage only very slightly infiltrated, being therefore but little raised above the surface. The redness, however, soon gives place to an opaque dulness, the layer of epithelium over the diseased spot changing to a bluish white, pearl-colored membrane which is more or less loosely adherent; the syphilitic papules of the mucous membrane are therefore also called *mucous patches* and *plaques opalines.*

Mucous patches usually have their seat on the mucous membrane of the lips or the cheeks, on the tongue especially on its border and tip, also on the lingual tonsil, on the soft palate, on the faucial tonsils, or in several of these localities at the same time, and in rare cases also on the posterior wall of the pharynx.

When the papules are situated partly on the skin and partly on the mucous membrane, as on the lips and angles of the mouth, they will vary in appearance according to the locality, assuming the characteristics of mucous patches when on the mucous membrane, and those of cutaneous papules when situated on the general integument. When the mucous patch undergoes resolution, the bluish-white membrane is first thrown off from the centre; the red papillary layer covered only with a thin epithelial skin then appears; the sharply defined whitish border at the periphery will be preserved for some time, but finally this also disappears and gives place to a normal epithelial layer.

In neglected cases, however, the infiltration of the mucous papule usually increases, it becomes more voluminous and is markedly raised above the surface. We then find larger, some granular bright red and glistening, and some whitish nodules, which are frequently closely packed at the border of the tongue and on the tonsils, and become very painful on account of the great inclination in these parts to become fissured. Destruction of the surface may occur here also, as in the weeping papule of the skin, and thus form *ulcers* which, when the ulceration is progressive, increase in depth and area and bring about a marked loss of substance.

As a result of the great irritation produced in chewing, smoking, etc., the mucous patches are quickly deprived of their epithelium, which on account of its natural moisture soon becomes macerated, loose, and is so thrown off.

The papule denuded of its epithelium is then seen glistening and red, and the surface breaks down pretty rapidly, so that a small ulcer

very soon makes its appearance, the base of which is formed by necrotic tissue. The ulcers become deeper and deeper, and we find by the side of reasonably large, succulent papules, especially on the tonsils, others which have been transformed into quite large and deep ulcers.

Another change in the appearance of the papules of the mucous membrane takes place in consequence of lacerations occurring in those portions which are subject to much movement; hence arise the *fissures* which are frequently observed at the angle of the mouth, the edge of the tongue, in the space between the tongue and the anterior arch of the gums, etc. These fissures and cracks, which are also observed in papules which are but slightly infiltrated, frequently cause great pain in chewing and talking, as also when they are brought in contact with irritating food.

The coalescence of several papules causes considerable swelling; the tongue will then hardly have room behind the teeth, which indent its border, and the tonsils when affected frequently stand out as far as the median line, touching each other, and offer a very grave obstruction to the passage of food. A tongue or tonsil swollen in this manner permits very plainly the recognition of the closely packed, partly solid, partly fissured and ulcerated papules. They are generally so closely packed on the soft palate, but especially on the uvula and the arches of the gums, that, in the latter case, for example, the anterior arch of the gum protrudes into the mouth in the form of a swollen, bluish-red or opaline, hard ledge, with its free border forming a sharp edge. Larger, closely packed papules of the mucous membrane may, however, flatten themselves against each other, assuming the appearance of swollen, reddened ridges, covered with cloudy epithelium. The papules of the mucous membrane of the oral and pharyngeal cavities are frequently accompanied by *swelling* of the *lymphatic glands* in the vicinity of the lower jaw and of the neck; this is painful only in the early stage.

Occasionally the papules within the oral and pharyngeal cavity represent the first visible symptoms of constitutional syphilis, and their appearance is sometimes ushered in by fever. They are frequently developed on an erythematous eruption of the mucous membrane and are observed accompanying the primary skin syphilides. The further course of the mucous-membrane papule does not, however, necessarily run parallel with that of the cutaneous syphilide.

When cleanliness is practised the opaline plaques will disappear in from two to four weeks, without leaving a trace, while the ragged, ulcerated papules, which are not kept clean, as well as those that are irritated by tobacco smoke and snuff, by stumps of teeth, and other

irritating matter, not only persist for weeks and months, but are also subject to frequent recurrences, as a result of these causes.

Recurrent papules of the lips, the tongue, the mucous membrane of the oral cavity, the soft palate, and the tonsils belong, very likely on account of the many irritations to which these parts are subjected, among the common symptoms. The papules recur, during the first year after infection or even later, with extraordinary obstinacy, even when every symptom of syphilis has long ago disappeared from all other parts of the body.

The later recurrences are usually confined to a few papules, at times even to one plaque, which may also disappear quite rapidly, to be replaced, however, just as rapidly by another patch in a different locality. The papules of a later syphilis show less marked infiltration and development towards the periphery, and tend to absorption at the centre; in this manner very slightly raised annular plaques are produced, which form the most peculiar serpigines by intermingling. These recurring papules are most frequently observed on the tongue and the lips; they are, however, also met with on the hard palate, the velum, etc.

On account of their location the papules of the buccal cavity are very dangerous to healthy persons who live with these patients; for it is almost inevitable that the secretions of these products should contaminate the eating- and drinking-vessels and other objects which are brought in contact with and into the mouth, and should thereby infect other persons using these utensils; or infection may be directly produced by contact, as in kissing. The danger of infection may be called constant when frequent recurrences cause the papules to appear again and again in various parts of the mucous membrane.

The lingual tonsil is affected quite frequently, as a rule together with the other organs of the pharynx, mucous patches being especially common here. Smooth atrophy of the base of the tongue is very often met with in syphilis.

The upper part of the *œsophagus* also belongs to the points of predilection of the gummatous deposits, so that, in the great majority of syphilitic patients, we shall hardly miss characteristic changes in these localities, which will point to still existing or passed processes.

Gummata.

Diffuse gummatous infiltrations are also encountered in these cases in addition to the circumscribed gummatous foci. The latter present themselves as nodes the size of a lentil to that of a pea or bean or still larger, and usually affect the submucous tissue, that is to say,

the mucoperiosteal membrane, more rarely the true mucous membrane or the more deeply lying structures.

The gummatous nodule makes itself apparent by an outward bulging, over which the mucous membrane is seen to be distinctly reddened. At first it is quite firm to the touch; later, however, it becomes soft and leads to ulceration as a rule, when the products of disintegration, the epithelial covering having already fallen off through maceration, very soon find their way to the outer world through the attenuated mucous membrane.

It may perhaps be due to the low resisting-power of the mucous membranes that the gummatous deposits usually break down and lead to the formation of ulcers of different degrees of area and depth; we know it to be a fact that gummatous infiltrations are much more rarely absorbed in this location than elsewhere, and that most of the gummata here go on to ulceration. The ulcers present various peculiarities according to the seat and distribution of the infiltrations. They may be superficial or deep-seated, isolated or confluent, round or elliptical, oblong or serpentine. As a rule, the border of the ulcer as well as its base is firm, villous, covered by a discolored deposit; the parts about are frequently occupied by an infiltration, which as a rule is sharply defined, and gives the mucous membrane, wherever the infiltration extends, a slightly red tint.

These ulcers are essentially chronic and may even increase progressively in area or depth, because the infiltration usually persists a long time, or even increases on the surface or towards the deeper structures. The process comes to a standstill only under a proper treatment. As the infiltration is not renewed, and that which is already present is partly absorbed and partly broken down and removed, the increase in circumference and in depth ceases. The ulcer is first observed to remain stationary, then it clears up, and finally approaches a cure. The cicatrices and lesions left behind frequently lead to notable distortions and deformities.

As a rule, the gummatous process in the buccal and pharyngeal cavity is exceedingly sluggish as regards the individual foci of infiltration, and also as regards the formation of new gummatous nodules during the presence or after the healing of the old ones. In rare instances only the course of the gumma becomes acute, so that within a few days frightful destruction may take place, such as ordinarily would not have occurred until after the lapse of months and years.

The *corners of the mouth*, the *lips*, and the mucous membrane of the *cheeks* do not frequently become the seat of gummata. When once established, they lead to extensive loss of tissue, so that the angle of the mouth or a large portion of a lip may be destroyed in a short

time. In a case of this kind the patient is hardly able to prevent the dribbling away of saliva and the dropping away of the food which has been taken into the mouth. It is only by great trouble and holding the head in proper position that food and drink can pass down, and accompanying this the swallowing of pus and other products of disintegration can hardly be prevented. The patients become debilitated in consequence, and are at the same time threatened with a hemorrhage from an erosion of the coronary artery of the lips. In one of my cases a hemorrhage producing syncope had occurred before the patient was brought to the clinic.

Although these gummatous ulcerations occur in conjunction with similar ulcerations of the face and neck, and only increase somewhat the repulsive appearance, still a properly conducted treatment will as a rule prevent great disfigurement, even after important lesions have already made their appearance.

Destruction of the upper lip by an independent gumma which has not invaded the part from the neighborhood is even more rarely observed. In a case belonging to this category I saw the totally destroyed lip replaced by a short, narrow, cicatricial band, towards which the septum narium was drawn downwards, while the angles of the mouth were drawn upwards, so that the oral fissure had been transformed into a round opening the size of a cherry, through which the exposed incisors could be seen. The size of the opening could be only very slightly increased. Gummatous processes of the upper lip, which accompany those of the neighboring parts of the nose, may be frequently observed.

Gummata of the *tongue* are quite frequently met with; the infiltration is rarely diffuse, in general it makes its appearance in foci. One or more nodules may be felt as firm tumors in the substance of the tongue near its upper surface, which are covered by smooth mucous membrane; in their further course the foci become softened and after rupturing discharge a thin, brown, sticky, more or less flocculent fluid; there is left behind an ulcer with rigid walls, the base of which occasionally rises above the surrounding level as an *ulcus elevatum*. The surface of the rest of the tongue is sometimes uneven, knobby, and fissured, at other times smooth. The affection is frequently very tender to the touch and on motion. A swelling of the neighboring lymphatic glands is rarely observed in connection with gummata of the tongue.

When proper treatment is instituted absorption of the infiltrate with healing of the ulcer very promptly results; if left to itself, the process is extremely sluggish, and may even terminate in carcinoma, as Hutchinson, B. v. Langenbeck, and myself have observed.

I have several times observed gummata of the mucoperiosteal membrane of an alveolar process, especially in the *upper jaw;* as a rule, the involved teeth become loosened and fall out; but we should not be in a hurry to remove them, as they may become fixed again should the process heal. When necrosis of the alveoli occurs, it goes without saying that the teeth will be lost.

The *hard palate* is much more frequently attacked by gummata, and these generally also lead to exposure of the bone, which frequently becomes perforated, thus producing a communication of the oral with the nasal cavity of greater or less extent.

The infiltration is at times observed as a fungoid growth on the alveolar processes of the teeth, thus forming as it were an *epulis syphilitica.*

I have seen a number of cases of syphilis of the upper jaw, but have rarely met with the disease in the lower maxilla.

The duplication of mucous membrane forming the *soft palate,* together with the thin muscular layer, as well as the palatine arch and the uvula, are quite frequently the seat of gummata, which stand out from the surrounding level in sharply defined outlines as rigid, disc-like infiltrations or as nodular tumors of various sizes, covered by a bluish-red mucous membrane. Owing to the thinness of the structures attacked, destruction of the tissues is of very frequent occurrence. Perforations and defects accordingly are very common.

The gummata situated on the posterior aspect of the soft palate may remain undiscovered for some time, as they frequently make their appearance in small foci only, and therefore occasion the patient but little annoyance. When the course is somewhat more rapid, however, disintegration at once appears, when perforation of some part of the thin velum palati speedily occurs. As a rule the affection does not run its course altogether unnoticed, for the destructive process, owing to the thinness of the affected parts, runs a more rapid course than elsewhere, unless proper treatment is early instituted.

I once observed at a very early period (two months after the development of the initial lesion) an ulcerating perforation of the right half of the velum, the size of a pea, in a woman, thirty-two years of age, who had been treated locally at my clinic for one and a half months for a primary lesion of the left labium majus and one of the left tonsil. It is quite probable that a local excursion of the contagium from the initial sclerosis of the tonsil to the velum took place, and gave rise here to an infiltration which took a malignant course, owing to the anæmic condition of the individual.

Aside from the perforation already alluded to, ulceration of the free border may also occur, so that the anterior or posterior palatal

arch assumes a more or less notched appearance; or when the seat of the gummatous ulceration is in the neighborhood of the uvula, the latter becomes eroded at its base, so that the uvula dangles from one side; or the uvula becomes ulcerated at its margin or its tip. When the gummatous infiltrations become more extensive, destructive processes covering a great area frequently take place. Loss of one or the other palatine arch, of the uvula, or even of the whole soft palate, may occur. If healing takes place at last, the soft palate after extensive infiltrations and superficial ulcerations presents a thin epithelial covering, the uvula a narrow strip, with lost muscular tissue and without any power of motion; or else we find cicatrization of the perforation and lesions or distortion of the soft palate and flexions of the uvula towards the side on which the ulceration previously took place—or a number of changes exist side by side which testify to the occurrences that have taken place here. Smaller perforations of the hard palate and larger ones of the velum may, moreover, be made to heal perfectly, if proper treatment is not attempted too late.

The *tonsils* are quite frequently the seat of gummatous ulcerations which are occasionally the cause of extensive destruction, so that only small remnants are left between deeply retracted cicatrices, or the tonsils may be altogether destroyed.

Diffuse gummatous infiltrations are observed more frequently on the posterior wall of the *pharynx* than in other localities. The wall of the pharynx then presents a bluish-red, slightly swollen appearance, covered with a tough, firmly adherent, purulent mucus, showing an erosion here and there; in milder forms the surface of the mucous membrane will be red, smooth, and shining, as if varnished. This condition causes the patient great distress in consequence of the dryness and rawness of the throat, and it is all the more annoying as moistening and gargling the parts afford relief for a few moments only.

Circumscribed gummata are more frequently encountered here, as are also the ulcerations of the pharynx caused by them, especially those of the posterior pharyngeal wall where these ulcerative conditions are most extensively seen.

In a certain number of cases the gummatous process advances to the bodies of the *cervical vertebræ* and leads to exposure of the bone, which occasionally becomes carious. Denudation of the *base of the skull* has been observed in cases in which disintegrating gummata developed on the spot where the pharyngeal sac is attached. This may be fraught with danger, for the reason that the base of the skull is thin and a deeply penetrating ulcerating gumma might easily reach

the cerebral membranes and the brain, and produce rapidly fatal complications.

Still other dangers threaten when large vessels become involved in the gummatous process, resulting possibly in grave and even fatal hemorrhage.

If gummatous ulcerations have become localized on the lateral wall of the pharynx, the contiguous portions of the Eustachian tube are in danger of being involved in the ulcerative process; this would be followed by a marked loss of hearing, and if narrowing, or, worse still, occlusion of the ostium pharyngeum tubæ should result from the process of cicatrization, permanent deafness might result.

In those cases in which gummatous ulcerations of the posterior wall of the pharynx occur, together with similar processes in the soft palate, and this condition is neglected, partial or complete adhesions of the soft palate to the posterior wall of the pharynx are not very unusual when cicatrization takes place. If the adhesions are extensive and the uvula is destroyed, the place of the latter will be taken by a triangular defect—the only communication between the upper cavity of the pharynx and the oral cavity—or the uvula remains as a shapeless cushion and plugs the opening just described; or the nasal cavity and the upper pharyngeal space are completely shut off from the lower pharynx and the oral cavity by a complete adhesion of the velum to the posterior pharyngeal wall.

As the oropharyngeal cavity may for years be an elective locality for the exhibition of syphilitic processes, we not infrequently find traces of an old syphilis by the side of recent gummata, as, for example, numerous cicatricial formations on the posterior pharyngeal wall and loss of the uvula, together with recent gummatous ulcers and infiltrations on the hard palate and on the remnants of the soft; or in a case of old adhesions of the soft palate and the posterior pharyngeal wall and cicatrized ulceration of the uvula, we may occasionally catch a glimpse through the perforations of a recent ulceration of the superior pharyngeal space, and discover a recent gummatous nodule behind the palatine arch. Gummatous nodules situated deep down in the pharynx can be recognized only with the aid of the laryngeal mirror; this examination will be facilitated by causing the larynx to move by means of phonation, in order to displace it from over the infiltrations, otherwise the gummata might easily be thought to belong to the posterior laryngeal wall.

The troubles caused by the gummata at the entrance of the digestive tract vary greatly; they may be very slight in cases in which the infiltrations cover only a small space and hardly enter into consideration. The distress is, however, so much the more marked the more

the parts on which the gummata are situated participate in the movements of chewing and talking. From this point of view the gummata situated on the tongue, the soft palate, the tonsils, and the posterior wall of the pharynx are frequently very annoying occurrences. The disturbances which result from a perforation of the hard or soft palate or from a partial or total adhesion of the latter to the posterior pharyngeal wall are very distressing. The food which is taken will then in great part enter the nasal cavity, and speech will acquire a so-called nasal tone, which becomes a permanent evidence of the disease through which the patient has passed. On the other hand again, the closed communication between the nasal cavity and the cavities of the mouth and the pharynx forces the patient to breathe with the open mouth, which gives to the individual a stupid expression, and besides causes an annoying dryness of the mouth and throat.

The healing process exposes the patient to great danger in those cases in which, in consequence of the slow course and frequent relapses of ulceration of the soft palate, a cicatricial ring is formed between the soft palate and the root of the tongue, or between the latter and the posterior pharyngeal wall. We then have to fear that the ring will become smaller and smaller in consequence of the progressive contraction of the cicatricial tissue, and that the soft parts external to it (mucous membrane and the muscular tissue which it may contain) will be drawn towards it. In this manner a membranous diaphragm is formed, which is either spread out between the oral and pharyngeal cavity, or separates the upper pharyngeal cavity from the lower and from the entrance to the larynx.

The defects in this diaphragm may be oblong or round; in the first case the opening usually lies in the median plane, in the latter occasionally to the side. If the perforation is large enough, perhaps allowing the insertion of a finger, there will be sufficient room, according to the location of the partition, for air or for nourishment to pass. It may then be noticed in isolated cases that the opening is contracted or widened by muscular contractions of the parts around the diaphragm. In the course of time, however, the opening in the membranous partition contracts more and more, as a rule, and it may even be diminished to the size of a pin's head, and constantly threatens the life of the patient by the great obstruction which it offers to the entrance of food and air. Cicatrices of this kind, which are also painful to the touch, and may even occasionally cause vomiting, are at times merely the result of an old syphilis, or they may be accompanied by recent ulcerations in the neighborhood. Complicating affections of the larynx are quite frequently encountered, but even in those cases in which the larynx is found to be perfectly healthy there

may be more or less marked aphonia, but the voice usually recovers its tone immediately after dilatation of the stricture.

Affections of the *salivary glands* occurring in the course of syphilis have been observed several times by myself and others.

Diagnosis.

If we bear in mind the description of the various processes as given above, the recognition of localized syphilis of the mouth and pharynx will not be connected with any great difficulty in the majority of cases.

An *initial lesion* may occur in this region at times in the form of a papule, at times as a plainly developed sclerosis with erosions and ulcerations, and again as a superficial erosion situated on a base not at all, or only slightly indurated. When situated farther back than the tonsils, they will be found only on the posterior surface of the velum and on the Eustachian tubercle, in which localities they can be seen only by means of the rhinoscope.

The initial affection will be followed, as in other places, by indolent enlargements of the neighboring lymphatic glands, and later by constitutional syphilis. If we will now bear in mind, besides the changes *in loco*, the succession of symptoms, the primary character of the affection is easily determined, and we may also be able frequently to discover the manner of infection.

Syphilitic *erythema of the mucous membrane* is sufficiently characterized by its principal location on the soft palate, the tonsils, and the pharynx, and by the frequently sharply defined hyperæmia, slight induration, and bluish borders of the patches.

The *papules* of the mucosa are easily recognized by the sharp outlines, the elevation, by the reddened or bluish-white epithelial covering, looking as though cauterized by nitrate of silver, as well as by the fact that they appear single or at times multiple and closely packed, here leading to fissures and superficial ulcerations, there to deep ulcerations; furthermore they may occasionally heal very rapidly.

The *gummata* are characterized by infiltrations which are usually sharply isolated but are frequently also diffuse, often causing destruction and perforation, and nearly always cicatrices, which latter are more or less delicate, according to the amount of destruction which has taken place, or which may be radiating, in which case they draw on and distort the soft parts.

As, however, the symptoms are not always sufficiently marked to prevent possible confusion, we may mention those diseases which might at times be mistaken for syphilis.

Acute stomatitis and *catarrhal sore throat* present a diffuse erythema and marked swelling, and are usually, even those accompanied by fever, of short duration.

Tonsillar abscesses are extremely painful and give evidence of distinct fluctuation. I have, however, frequently observed such abscess formation in syphilis of the tonsils. It is quite probable that the acute inflammation in these cases is a result of the ulceration, whereby opportunity is offered for the entrance of germs exciting inflammation.

In cases of *chronic catarrh*, as it is found in drunkards, smokers, snuff-takers, etc., we may readily arrive at a satisfactory diagnosis by the discovery of the causative factor, which we can find usually at the cost of a little attention.

Herpes of the mucous membrane of the mouth (*stomatitis herpetica*) leads to the formation of small, sharply circumscribed, superficial ulcers, rarely attaining a size larger than that of a pin's head, which are situated on a reddened mucous membrane, and generally arranged in groups. Herpetic ulcers are met with on the mucous membrane of the lip and the cheek, on the tongue, and also as far back as the posterior pharyngeal wall (*angina herpetica*). We may also remark that herpes of the mucosa runs as rapid a course as the same eruption on the skin, and is subject to relapses just as frequently. The appearance at the same time of a similar eruption on the skin simplifies the diagnosis greatly. We must not forget, however, that individuals who have passed through venereal affections not very rarely present herpetic eruptions on the genitals or in their neighborhood. Where herpes makes its appearance at the same time in the mouth and on the genitals, we shall have to devote much greater care to the clinical character of this vesicular eruption. In a few isolated cases I have noted the occurrence of *erosions* on the tongue, lips, cheeks, or gums, of the size of lentils and still larger, seated on a slightly indurated base; they were of a vivid red color or were covered with a white deposit, and then resembled very closely eroded papules, so much the more as the same changes were also to be seen on the genitals (glans, preputium, scrotum), except that at the borders of isolated erosions of the scrotum the remains of vesicles were visible. This fact, as well as the observation that relapses always occurred in the same form and —what is conclusive—that an exactly similar affection was discovered in individuals who had never contracted syphilis, influenced me to diagnose a local relapsing vesicular eruption, which was independent of syphilis. Whether this is to be looked upon as an erythema, as O. Rosenthal maintains, or as a case of benign pemphigus, I am unable at present to say.

Besides the last-named vesicular eruption, *pemphigus papillaris*

vegetans, which makes its appearance with especial predilection on the lips and the alæ nasi, and at the same time on the anus, the genitals, or in the genitocrural folds, might by superficial observers be taken for syphilis, for the reason that the base of the vesicle frequently enlarges as a plaque and appears like a papilloma. It will, however, not escape the careful observer that the plaques are surrounded by vesicles, and that well-characterized plaques are also developed on other parts of the body. A mistake in diagnosis would be a serious matter, for pemphigus vegetans often ends in death.

In women a *benign stomatitis* accompanied by shallow ulcers is likely to accompany lactation (*stomatitis materna* of the ancients), or pregnancy, or menstruation, or various pathological conditions of the uterus (we might here speak of a *stomatitis uterina*).

In children *thrush* is readily recognized by the presence of white membranes, either punctiform or of wider extent, which show under the microscope thallus threads and spores between the epithelia, and are easily recognized by their acid reaction; in adults these fungus colonies are met only in progressive cachexia, and they foretell an early fatal issue.

Venereal ulcers of the lips and in the neighborhood of the oral and pharyngeal cavities are extremely infrequent; Ricord did not see a single instance in his practice of forty years.

A stomatitis accompanied by fever is occasionally developed, sometimes sporadically, sometimes in an epidemic form, and is accompanied by marked swelling and pain of the greater part of the mucous membrane of the mouth; after a few days extensive but shallow ulcers appear on the cheeks, the tongue, and at the vermilion border of the lips, which are covered in the oral cavity with a whitish deposit, on the vermilion border of the lips with thin brownish crusts; secretion is increased,—at first it is seromucous, later purulent; the odor from the mouth is fetid. The affection is known as *stomatitis ulcerosa* or *stomacace*. A proper local treatment as a rule brings about a rapid cure.

An affection of the mouth, resembling ulcerating stomatitis, occurs in foot-and-mouth disease. This *stomatitis aphthosa epizootica* is frequently accompanied by an eruption on the hands and feet and occasionally also on other parts of the body.

The absorption of mercury, usually in its medicinal use, in the form of inunctions, subcutaneous injections, internal preparations, etc., or after cauterization, leads in many persons sooner or later to an inflammation of the mucous membrane, accompanied by a greatly increased flow of saliva (*stomatitis mercurialis*); this generally causes swelling of the gums, and occasionally also inflammatory swelling of

the cheek and tongue in such a manner that the rows of teeth leave their imprint in them. The patient complains early of a metallic taste, and the fetor ex ore is marked and increases when ulceration occurs on the tongue, lip, or cheek. These ulcers, *mercurial ulcers*, are shallow, covered more or less with a deposit, and surrounded by an inflammatory redness. The careless administration of mercury leads only to extensive necrosis of tissue and to denudation and necrosis of the jaw.

Occasionally we see on the mucous membrane of the cheeks and lips, more rarely of the hard palate, punctate, linear, or irregularly outlined, opaque, milk-white spots, looking as though they had been touched with a stick of nitrate of silver (or sometimes of a steel-gray color) which in contrast to the otherwise smooth and soft mucosa are wrinkled and have a tough, callous, leathery feel, giving to the touch the sensation of tanned skin.

Similar changes are found in combination with these or alone on the back and borders of the tongue, but differ from them in that the diseased parts are in various forms and distribution, at times smooth, at times fissured and bare of papillæ, while the rest of the tongue is somewhat thickened, studded with elongated papillæ filiformes, and covered with a viscid mucus; the papillæ filiformes occasionally protrude as swollen nodules, dotted with red and bare of epithelium. Clefts and fissures, which are rarely absent from the tongue in this disease and are met with less frequently on the mucous membrane of the lip and cheek, are frequently the cause of much pain and lead to the formation of shallow ulcers. This condition, which has been described as *ichthyosis linguæ* (Samuel Plumbe), *tylosis linguæ* (D. Ullmann), *psoriasis linguæ* (Bazin, Sigmund, Kaposi, M. Nedopil), *keratosis linguæ* (Kaposi), *plaques lisses* (Fournier), *leucoplakia* (Ernst Schwimmer), is characterized by an extremely chronic course, and has only in exceptional cases been seen in women. Robert F. Weir, however, found the labia majora and minora changed in a similar manner in one case. In one or two cases this alteration in the mucous membrane proved to be the beginning of a carcinomatous neoplasm.

According to my experience, these plaques are most frequently observed in the course of habitual indigestion, and in smokers, according to Seegen, also in diabetic patients. Tobacco smoking seems to be looked upon by several authors as the most prominent etiological factor (*plaques des fumeurs*, of Buzenet). According to the view of many authors the occurrence of these callosities of the mucous membrane is directly caused or else favored by syphilis. I myself cannot but believe that a past or still present syphilis is a predisposing factor in the development of leucoplakia.

Very frequently the following changes found on the tongue may impress one as those of syphilis: Various sized, isolated or confluent, red spots, not at all or only slightly infiltrated, are sometimes observed on the border and at the tip of the tongue, less frequently on the back and under surface, which are surrounded by a sharply defined, narrow, dirty white or clay-colored epithelial border. These plaques are continually on the increase, or, as I have frequently observed, disappear altogether to reappear again, after a longer or shorter period; they do not cause any annoyance unless they should lead to erosions and ulceration. I have several times observed these spots on the tongue in children and in adults in cases of indigestion. Alterations of the intestinal tract and a lowered nutrition (anæmia) seem in fact to bear some relation to these plaques in most cases. Parrot has observed them in thirty-one children, and connects them with hereditary syphilis, hence also his designation, *syphilis desquamative de la langue.* The other names of the affection mostly refer to the external appearance and sometimes are borrowed from the seemingly analogous processes of the skin, psoriasis or pityriasis linguæ, lichenoid desquamation, lingua geographica, exfoliatio areata linguæ, and desquamation épithéliale de la langue. It will always be difficult to exclude syphilis at once by inspection alone, and we shall be justified in doing this only after a longer period of observation and after taking into consideration other symptoms. These desquamations are just as little influenced by an antisyphilitic treatment as the callosities before mentioned.

Finally it should be pointed out that the tongue is sometimes shaggy, greatly furrowed, or occasionally smooth on its upper surface and at its border in individuals who are otherwise in perfect health. I have named such a tongue, which may be looked at by the inexperienced as diseased, *lingua plicata.* Although we are not dealing here with a pathological condition, but only with an anomaly, it can be readily understood that if pathogenic germs are deposited in these folds they will be more likely to form permanent colonies and to induce pathological changes, than when they are deposited on a tongue with a smooth surface. Accordingly not infrequently erosions and shallow ulcers are here established, which heal with difficulty, because the germs deposited are not easily destroyed by local medication. Syphilitic plaques occurring on a lingua plicata also resist treatment longer than otherwise.

Among other grave processes, which like syphilis lead to chronic processes of infiltration, to disintegration and loss of substance, to cicatricial scars and strictures, may be mentioned *lupus.* This disease, when occurring within the oral and pharyngeal cavity, most

closely imitates syphilis. It occurs as a rule as a pale red, or purplish-red, granulating, ulcerated surface, by the side of which occasionally cylindrical outgrowths, for example on the gums and the tonsils, form nodular swellings. These spots, covered with a thin epithelial covering, as well as the small foci of lupus of the mucous membrane which have not yet become ulcerated, are in strong contrast with the surrounding healthy parts by their bluish glimmer. The lupous infiltrations are as a rule soft to the touch; they produce extensive lesions only in the soft parts, generally only after years, while perforations occur on the bones, most frequently in the processus palatinus, immediately behind the teeth. The fact that the disease begins usually at an early age and takes its origin from the external integument, is very important in the diagnosis of lupus; we shall, therefore, when lupus is located in the oral and pharyngeal cavity, almost invariably find distinctly marked lupus, or cicatrices which it has left behind, on the face. We are, however, to bear in mind that lupus may also occasionally have its beginning on the mucous membrane.

Acute (miliary) *tuberculous ulcers*, which are found on the tongue, the palate, and the wall of the pharynx, sometimes primary, sometimes combined with tuberculosis of the lung, the intestinal canal, the lymphatic glands, or other organs, may very easily be confounded with syphilis. In marked cases the tuberculous ulcers will present a cheesy, lardaceous, and undermined sloughing border, of a bluish-red color, and studded with miliary nodules; these same nodules are also found in the mucous membrane of the immediate vicinity, which, originally covered with smooth epithelium, will later become the seat of the ulceration. Tubercle bacilli can often be demonstrated in the discharge or in the miliary nodules which have fallen or which have been picked out. The ulcers commonly originate on the tonsils or the mucous membrane of the vault of the pharynx, but frequently also extend from the walls of the pharynx to the velum, or to the posterior pharyngeal wall, where they often assume an oblique position, and rarely show a tendency to undermine the surrounding surface; as a rule they extend superficially only and are sharply limited at the beginning of the œsophagus (Fraenkel).

Where the velum is involved the uvula is either spared, in which case it will appear thin and atrophic, or it will be transformed into a shapeless swollen mass by the tuberculous infiltration; Fraenkel also points out an inclination to hypertrophy, especially in the tonsils, where polypoid excrescences are apt to occur. Extension to the border and back of the tongue is frequently observed; but the border or tip of the tongue may be the primary seat of the tuberculous ulcers.

In a few cases larger, firm tuberculous nodules are also found together with the lingual ulcers. In a patient under my care a very painful tuberculous ulcer of the tip of the tongue led to a fatal issue with typhoid symptoms in a few days. At the post-mortem examination a miliary tuberculosis of the lungs, the kidneys, the liver, and the spleen was found. Tuberculous ulcers are frequently characterized by their extreme painfulness, which, already existing spontaneously, may be so increased when the ulcers are touched that every attempt to take nourishment becomes agony; occasionally the process is accompanied with high fever. These conditions as well as the probable involvement in the tuberculosis of other organs, as the larynx, the lungs, the testicles, etc., conspire to the rapid decline of the patient, so that it will not be difficult to recognize the tuberculous ulcers, even when tubercle bacilli are not at once found.

In consequence of the near relation which exists between chronic tuberculosis (lupus), acute (miliary) tuberculosis, and scrofula, and of the various transitions of these conditions into each other, it may in isolated cases be very difficult correctly to interpret the nature of an acute or chronic infiltration of the mucous membrane of the oral and pharyngeal cavity which goes on to ulceration; the finding of tubercle bacilli (which are only sparsely present in lupus) is of great diagnostic importance in tuberculosis; otherwise we are of necessity confined to the observation of the further course of the disease and to the results of treatment. The difficulty in the diagnosis is still further increased when syphilitic deposits become later tuberculous, or when syphilis is complicated with a previously existing tuberculosis.

As regards *leprosy*, which is found only in certain parts of the world, we must remember that it much more frequently causes affections of the mucous membrane resembling syphilis than those involving the outer integument.

Easy as it is in most cases to distinguish gummata from tumors, especially in their later stages, yet in individual cases the diagnosis becomes extremely difficult.

The mucous membrane of the lips and cheeks is occasionally the seat of benign *papillomatous* growths, covered by a more or less dense, whitish or bluish-white epithelial layer, which as a rule persist unchanged for years, but sometimes gradually disappear when painted with a weak arsenical or sublimate solution; the inexperienced not infrequently mistakes these excrescences, which are, however, only rarely observed, for syphilitic products. Less often we see on other portions of the mucosa of the mouth and pharynx, most frequently on the soft palate and the tonsils, *papillomata*, which, like the other

forms, especially those occurring on the genitals, must be looked upon as due to a long-continued irritation. I have qualified these papillomata as venereal, because they are as a rule developed in the course of gonorrhœa, occasionally, however, also with and following syphilitic affections—therefore, as a general rule, on venereal soil. They appear from the size of a pin's head to that of a pea and still larger, are pedunculated or sessile, and when examined by the probe prove to consist either of dendritic arborescent growths, or of palissade-like cylinders of equal size; their surface is red or of a dull white color, according as the epithelial layer is thin or as there are several layers present; they readily bleed, but do not ulcerate.

Carcinoma of the lips can be mistaken only in the beginning for an initial lesion which is frequently seen in this locality; the latter is, however, accompanied very early by indolent enlargements of the lymphatic glands, and the results of the local use of mercury are striking.

Very frequently we are called upon to make a diagnosis between carcinoma and syphilis of the tongue. Syphilitic initial lesions of the tongue are very soon followed by an enlargement of the neighboring lymphatic glands; in carcinoma these complications as a rule occur later. Gummata of this organ generally develop below the surface, and frequently in several places, either at the same time or following each other; carcinoma usually has its origin on the surface generally as a single tumor; gummata rarely involve the surrounding tissue. This is, however, one of the characteristics of cancer. If the neoplasm spreads over the surface as a fungoid growth, the supposition of a carcinoma is rendered more probable; more than one observation, however, proves that a gumma may assume a like appearance. Finally, I would remind the reader once more that, as already mentioned, Hutchinson, Langenbeck, and myself have observed the transformation of gummata into cancer or the existence of these processes on the tongue side by side.

In spite of the most careful study of all conditions we shall in rare cases be unable to distinguish between a malignant tumor and a gumma in other localities, and only continued observation will make it clear to us whether, for example, a deposit of the tonsils should be looked upon as a sarcomatous or syphilitic process, or whether a growth of the gum should be considered an epulis or a gumma. Certain superficial carcinomata (on the mucous membrane of the cheek, the hard palate, etc.) cause us to hesitate the longest, for they appear in the beginning as benign ulcers, and only after from one to two years throw off their mask of innocence and—alas, too late!—disclose their full malignancy. I might mention many cases in which the

favorable time for the radical removal of a superficial cancer was frittered away by useless antisyphilitic treatment.

Of the rarer affections of the tongue I will only mention those which are liable to be mistaken for syphilis; and first *glossitis cicatrisans*. I understand by this a creeping affection of the tongue accompanied by the formation of cicatrices, which causes loss of the papillæ and of the mucous membrane in its whole extent, in places even destruction of muscular tissue; the tongue appears perfectly smooth in some parts, in others scarred and contracted, and, as far as the diseased region extends, as though covered by a membrane of the thinness of a spider-web, which is eroded only here and there; with this there is rarely a distinct infiltration, the tongue is rather soft to the touch throughout its whole extent. Occasionally only a small portion, maybe a spot of the lingual border the size of an almond, at another time a larger portion of the whole tongue, is affected in the manner described. As long as erosions are present the affection is extraordinarily painful; every movement, each contact with food, especially if the latter is highly seasoned or warmer than usual, increases the pain enormously; while this condition lasts a great deal of saliva usually gathers in the mouth; the anxious fear of the patient of movement on the one hand, and on the other the accumulation of saliva, lead to a peculiar clumsiness of speech, which is at once remarked. When no erosions are present, tenderness is only slight, sometimes altogether absent. Nothing positive can be said of the etiology of this glossitis; it is possible that antecedent lues may be a disposing factor, but I have met this same disease also in individuals who had never contracted syphilis.

Occasionally we meet with shallow *ulcers* of the tongue, of whose nature we are ignorant; it is most likely that we have to deal here with a growth of microorganisms that have not yet been closely studied. This, at least, was the explanation I was obliged to give of a superficial nearly circular ulcer of the tongue in a man who did not give any signs whatever either of tuberculosis or of lues.

Acute inflammations leading to *abscess* are likely to give rise to mistakes only because of their peculiar localization on the tongue and because of their relative infrequency; abscess of the tongue will seldom remain unrecognized for any length of time, but the diagnosis in the case of a chronic abscess may be more difficult.

Actinomycosis has also been observed on the tongue, and we should therefore not forget the possibility of its existence in any given case.

The Gastroenteric Canal.

Frequent as are syphilitic processes at the entrance of the digestive tract, and manifold as they are in form, in just such proportion are syphilitic affections rare in the continuation of the intestinal tract, excepting the rectum, of which we shall speak later. Of irritative forms of disease we know practically nothing; although the œsophagus and stomach have been brought under closer inspection in recent times (by the œsophagoscope and gastroscope of Mikulicz), we do not feel the necessity of exploring these parts in early syphilis, on account of the absence of annoying symptoms. But even when lues exists for some time, we are only very rarely placed in a position to demonstrate lesions of the œsophagus.

Among the various causes of dysphagia, which may arise in part in a reflex manner, in part from the irritation of neighboring foci of disease, we may occasionally find syphilitic processes of the pharynx or larynx; I have for example seen difficult deglutition in a case of cervical spondylitis. Neurotic dysphagia from paralysis of the *œsophagus* has been observed in the course of syphilis and has disappeared under antisyphilitic treatment (Wilson). A very few cases of cicatricial narrowing and gummatous infiltrations and ulcerations have, however, been demonstrated by anatomical and clinical observations. Cases have also been recorded, in which obstruction to deglutition in the œsophagus has been cured, or at least improved, by the internal exhibition of iodide of potassium, iodide of iron, etc. When cicatricial contractions have, however, once been formed, they remain a bar to improvement; or the symptoms of cicatricial contraction will appear only a long time after recovery from lues. In several cases (Maury, Bryant) a syphilitic stenosis even necessitated the performance of gastrostomy. We shall therefore be obliged, when an obstruction of the passage of the œsophagus occurs in an individual who is proved to have suffered from syphilis, or is still suffering from it, to think of its probable connection with this constitutional disease, the more so the less we are able to find any other cause for the presence of the dysphagia. The diagnosis may, however, at times be accompanied with great difficulty. Podrazki was induced in one case by the accompanying symptoms and the antecedent affections to diagnose a syphilitic stricture of the œsophagus, and yet a carcinoma was found at the autopsy (A. Weichselbaum); there may have originally been a gummatous infiltration in this case which furnished the soil for a carcinoma.

If syphilis of the œsophagus is discovered early, a favorable issue

is to be expected. The prognosis is much more unfavorable when extensive destruction has occurred, for then permanent cicatricial scars will be left even after healing has taken place.

In recent times syphilitic affections of the *stomach* have been somewhat more frequently brought to our attention. From a clinical point of view an experience of Andral is very interesting. In an emaciated individual with a lead-colored skin, who complained of anorexia, painful sensations below the xyphoid process, frequent eructations, and vomiting of food a few hours after its ingestion, Andral suspected syphilis from the presence of an ulcer on the posterior wall of the pharynx, and cured his man by the exhibition of mercurials.

That affections of the *intestinal canal* are met with in lues was clearly demonstrated by the older writers on syphilis. Compared with the syphilitic affections of the stomach, those of the intestines are in fact somewhat more frequent, and the frequency is greatly increased if we include in this category syphilitic enteritis occurring in hereditary syphilis. Syphilis of the intestine has been demonstrated anatomically, accompanying the same affection of the stomach, and a few times occurring by itself. Peritonitis and perforation of the intestine by syphilitic ulcerations are rarely found.

Stubborn diarrhœa, which resists the usual remedies and is only cured by the internal exhibition of mercurial preparations, not infrequently occurs in early syphilis. It should not be forgotten, however, that enteritis (as we shall demonstrate later) may also develop during a mercurial course, as a symptom of hydrargyrosis. We must therefore determine carefully whether or not, in a particular case, the diarrhœa is due to the action of mercury. The possibility of this occurrence was remarked upon by some of the earlier syphilographers.

When we come to the *rectum* and *anus* we come to a region where the intestinal canal is again easier of exploration; and morbid changes are therefore more readily demonstrated here. As a matter of fact most of the changes occur in the lower part of the rectum.

Initial lesions have been not infrequently observed at the anus and higher up in the rectum, as well in men who were addicted to passive pederasty as in women who practised venus præpostica. I have seen the initial lesion here only in the form of an indurated chancre. This may ulcerate early and result in painful fissured ulcers, in consequence of the uncleanliness and dilatation which is unavoidable in these parts during each act of defecation; these fissures are just as agonizingly painful on defecation as the non-specific anal lesions. When proper treatment is instituted, a perfect cure may usually be expected; we can, however, very readily imagine that

an initial lesion occupying the anal ring or seated on the mucous membrane of the rectum is just as likely to cause a contraction as the analogous affection of the prepuce, which frequently leaves a phimosis behind.

In a widow, forty-two years of age, who permitted coitus per rectum in order to avoid pregnancy, I observed an initial induration both on the left labium majus and in the rectum, together with an indubitable rectal blennorrhœa. We should also in these cases be prepared to find paraanal initial lesions, on the perineum for example; I have repeatedly also found the initial lesion in the crena ani.

Irritative lesions of constitutional syphilis are said to be rare in the rectum, but they occur certainly more frequently than is believed. In those cases in which mucous patches occupy the perineum and the neighborhood of the anus, we frequently observe eruptions of one kind or another stretching out towards the mucous membrane, or we may see fissures and ulcers of the anal folds, which are studded with papules, encroaching on the mucosa. Syphilitic papules have also been observed further up on the mucous membrane of the rectum; in individual cases they may reach so large a size as to cause troubles similar to those resulting from cancerous stricture of the rectum; these lesions have frequently been observed to heal under an antisyphilitic treatment, and cases of the sort were reported as early as in Morgagni's time.

To determine the frequency with which syphilitic papules appear on the rectum, a few patients from my clinic affected with irritative symptoms of syphilis were methodically examined for this purpose. Of a total of 110 patients (45 males and 65 females) plaques were found in the rectum in 16 cases (3 males and 13 females). These were generally situated on the posterior wall, but occasionally also on the right or left side; in three cases they occupied the entire circumference of the bowel. Notwithstanding that the papules were ulcerated nearly without exception, still only three patients complained of pain on defecation, which was occasionally accompanied by bleeding; in one case tenesmus was present beside a copious discharge of mucus and pus. The plaques, which were situated high up in several cases, could with some care always be felt by a digital examination alone, which was verified in every case by the use of the gorget or some other instrument. As a rule the papules in the neighborhood of the anus had no connection with those in the rectum; in a few cases they were present in the rectum.

Gummatous affections of the rectum are frequently observed; they very often lead to ulceration and destruction of the entire mucous membrane, thus laying the muscular tissue bare, and this latter is

also riddled with ulcers and enormously thickened. A hemorrhagic exudation attended with ulceration may also be found in the glandular apparatus of the large intestine. In a case of the sort observed by me the disease process had increased in intensity towards the rectum and had led in the region of the internal sphincter to a complete loss of the mucous membrane and denudation of the muscular layer; during life, watery, bloody stools were present, together with moderate tenesmus and loss of the abdominal sensation, that is, involuntary passage of the stool. A digital examination in such a case would arouse suspicions of the presence of an ulcer because of the puffiness and irregularities of the mucous membrane. Similar changes have been observed in stricture of the rectum. The symptoms are proctorrhœa and pain in the rectum, on the one hand tenesmus, on the other involuntary passages alternating with constipation. If the ulcerating process heals, a stricture of the rectum with accompanying symptoms will only rarely be avoided.

If gummata which are situated in the perirectal tissue break down, perforation of the rectum, of the vagina, or externally in the vicinity of the anus may occur, and a number of fistulæ may be established in this manner (rectoperineal and rectovaginal fistulæ), which are accompanied by an ichorous discharge from the rectum. Besides this, strictures of the rectum are frequently observed. Ulcerating processes extending high up may give rise to peritonitis. In a case of dysentery and stricture of the rectum, reported by Samuel Wilks, an abscess developed at the crest of the ilium which communicated with the intestinal canal; at the autopsy cicatrices were found in the flexura iliaca. In the case of a female patient from my clinic we were able to enter a large general perirectal cavity through several fistulous passages, which were situated around the anus and the external genitals; besides this there were present stricture and a syphilitic ulceration of the rectum, extending far up. The rectum is, however, often also the seat of that form of infiltration which ends in contractions, which we have already studied in another place, as a *syphilitic callosity*, and which is probably identical with what Fournier calls "anorectal syphiloma." We are here dealing with an infiltration occupying the anorectal walls, which, changing into contracting fibrous tissue, transforms the rectum into a rigid narrow cylinder about 4 cm. long; the thickness of the walls may reach 1 cm. and mainly affects the ampulla; the neighborhood of the sphincter usually escapes. Involvement of the anus is noticed only when the process extends from the rectum, in which case the anal portion will present a lobulated configuration. The disease in the early period runs its course without attracting notice, and it is only after the contraction

has become marked that the symptoms of obstinate stricture make their appearance.

In conclusion I think it necessary to mention that rectal strictures undoubtedly occur much more frequently than we have hitherto believed as a result of a rectal blennorrhœa which has existed for years, and it is very likely that among the strictures of the rectum which were formerly ascribed to syphilis, many cases were included whose etiological factor lay in a blennorrhœa.

The Liver.

At the first epidemic appearance of syphilis, that is to say when the disease became generally known, an important rôle was assigned the liver in so far as, according to Galen's teaching, which at that time was authoritative, the cause of syphilis was ascribed to a "congestio excrementorum," for which only one organ, however, the liver, was made responsible.

Our knowledge of syphilis of the liver is based upon the work of Dittrich, in 1849, which was amplified later, anatomically and clinically, by Gubler, Virchow, Rokitansky, Bamberger, Frerichs, and others.

We distinguish between a diffuse and a circumscribed gummatous affection of the liver.

In *diffuse gummatous infiltration* a new cellular growth is met with everywhere in the interlobular connective tissue, following the course of the vessels; in portions where the newly formed cells are densely packed, they totally displace the liver cells surrounding the capillaries in the interior of the acini, and in this way cause their destruction. The liver is in nearly all instances enlarged, heavy, bloodless on incision, and has a more or less homogeneous appearance on account of the indistinctness of the acini. If the individual does not succumb, the tissue, rich in cells, is transformed into a contractile substance and cirrhosis also is not unusual. Diffuse hepatitis, therefore, which is frequently met with in hereditary syphilis, may in exceptional cases be the cause of cirrhosis in young persons (Rindfleisch).

Circumscribed gummata are found in the liver singly or in great numbers, from the size of a millet seed to that of a walnut and even larger, situated either on the surface of the organ, at its edges, or in the connective tissue of Glisson's capsule around the larger blood-vessels (Ferdinand Schott).

The gummatous product is in most cases surrounded by arborescent connective tissue, which passes through the organ in long bands, and is connected with similar bands surrounding other superficial or

deep gummata of the neighborhood. The gumma of the liver softens and becomes absorbed, or, what is more generally the case, it goes on to cheesy degeneration; the fibrous tissue surrounding the gummata retracts more and more in the course of time and leads to nodulation of the surface, indentation of the border, or contraction of the whole organ or part of it. Franz Riegel and Chvostek have described cases in which portions were cut off by contracting fibrous cords and were connected with the rest of the liver only by a cicatricial band. In many cases hardly a trace of the gummatous deposits remains, with the exception of small collections of caseous material, so that we can speak only of a *syphilitic callosity*. The liver tissue existing between the callous fibrous bands undergoes either amyloid or fatty degeneration; very often it has a normal aspect, or, as Frerichs has found, in agreement with Virchow, is hypertrophied in the sense of enlargement of the acini and liver cells.

As regards its size, the liver rarely keeps within its normal bounds. When the connective-tissue bands have much contracted, a marked diminution, even down to the size of a fist, may be observed; on the other hand, a marked enlargement of the organ is frequently found in cases of amyloid degeneration.

Signs of *perihepatitis* in the form of more or less heavy leathery layers of connective tissue are usually found on the convex surface, hence also adhesions with the diaphragm are more frequent, with the colon or stomach more rare.

Enlargement of the spleen, amyloid degeneration of the kidneys, lymphatic glands, etc., and their accompanying cachexias are frequently found, besides other grave symptoms of lues, as complications of syphilis of the liver.

That affections of the liver may also make their appearance occasionally in the early stages of syphilis can hardly be doubted now. Gubler and Leudet took the view that individual cases of *icterus* in the early stage of syphilis should be looked upon as the first sign of a syphilitic hepatitis. Moulard also believed in a peculiar form of icterus occurring in early syphilis. I have frequently observed jaundice (sometimes accompanied by tenderness on pressure of the liver) in early syphilis, and (together with Engel-Reimers, Lasch) have demonstrated that digestive symptoms do not always precede this phenomenon. The icterus usually disappears together with the syphilis. We can very readily believe that an erythematous swelling of the mucous membrane of the gall-ducts is in many cases the cause of the icterus (Senator). According to our apprehension of the relation of the pathological changes to the contagium of syphilis such an assumption seems permissible. Virchow also thinks it probable "that the

simpler forms are as a general rule the earlier ones, and that the gummata generally develop on the soil prepared for them by the former." The observation of Key, according to whom a gumma the size of a walnut and immediately by its side another of the size of a pea were found in the right lobe of the liver, in a girl who died of tuberculosis and who had been treated seven months previously for a genital ulcer, does away with any doubt concerning the early occurrence of disease of the liver in syphilis. Fleischhauer has reported an interesting case of icterus in a young man who was suffering from syphilis; the cause of the jaundice in this patient, who died of an intercurrent disease, was found to be a gumma of the porta hepatis. It may be that in some cases enlargements of the lymphatic glands of the portal vein are the cause of icterus (Engel-Reimers). It may, however, also be possible that an independent catarrh of the gall-ducts, or one extending from the gastroduodenal tract, like other diseases of the mucous membrane, is followed by a simple icterus, as the expression of an irritative syphilitic process, without a positive disease of the liver. Aside from this, we must, however, also admit the possibility that the contagium of syphilis, like any other infectious matter, may perhaps, by the products of its metabolism, act in such a manner on the parenchyma of the liver (and of other organs) that icterus is produced; we might very well speak in this sense of a toxic, namely, of a *syphilotoxic* icterus; it may be possible that it possesses a certain analogy with that form of icterus which a few clinicians (Kelsch, M. Heitler, Weil, N. P. Wassilyef, Arthur Hennig, and others) connect with an infection, others with ptomain poisoning (Chauffard).

The diffuse affection of this organ which presents the picture of an *acute yellow atrophy of the liver* has been observed several times in early syphilis by Oppolzer and others, and in syphilis in general by Frerichs and E. Neusser. Julius Engel-Reimers observed acute yellow atrophy of the liver in three cases of recent syphilis; from the colossal swelling of the glands on the hilus of the liver, which is absent in poisoning by phosphorus, he believed himself justified in assuming its connection with lues. Senator also records two similar observations, and lays stress on the marked diminution in size of the liver, enlargement of the spleen, cerebral symptoms, and especially the presence of tyrosin in the urine, which substance is very rarely found in cases of poisoning by phosphorus, and then only in small quantities. On the whole, however, well characterized syphilitic affections of the liver will probably attract the attention only after the contagion has existed for some time. Among Chvostek's patients the first symptoms made their appearance very long after the

initial lesion, at the earliest in two years, at the latest forty years after infection. The reports of most observers are similar to this. We must not, however, draw the conclusion that the beginning of the morbid changes occurs only in the advanced stages of the constitutional affection. It is, moreover, very probable that the first clinical symptoms frequently enough appear after the liver has already been affected for some time, for in the great majority of cases the initial symptoms are very obscure and indistinctly developed, and in individual cases the whole syphilitic process may even run its course in a scarcely noticeable manner, so that syphilis of the liver is found only by chance at the post-mortem examination. The symptoms may, however, also be more distinctly marked, and then will vary according to the seat, the extent, and the stage of the disease.

The patient very frequently complains of a feeling of discomfort or of heaviness in the region of the liver, especially when the latter is enlarged. Pain in this region quite frequently ushers in the disease; it is moderately severe and dull, or may be increased until it becomes unbearable. Its duration frequently covers months, with many intermissions, finally disappearing altogether with the further course of the disease. The pains very rarely radiate towards the shoulder. In most cases pain is due to perihepatitis; and we can then at times feel or hear *friction* over the liver, which is caused by the displacement of the roughened surfaces of the peritoneum with the movements of respiration. Sometimes the occurrence of friction sounds or feeling is prevented in cases in which the perihepatitis has led to adhesions.

The *size of the liver* is rarely normal. In cases in which we have been able to follow the whole disease process we are in position to observe the initial increase and later the gradual decrease in size of the organ. The detection on palpation of irregularities and nodules on the surface and of notches at the border are most characteristic signs of hepatic syphilis.

Icterus is very frequently absent in syphilis of the liver; when the larger ramifications of the gall-ducts or of the hepatic duct are themselves compressed by gummatous deposits or cicatrices, jaundice will occur, and will last some time, probably until the secreting portion is destroyed.

Ascites is more frequently met with, very often in cases of small liver, but also when the viscus is increased in size; this is the result of compression in the region of the portal vein. Now and again the obstruction within the area of the portal vein leads to *hemorrhages from the stomach and intestine.* Diarrhœas seem to be produced by an amyloid degeneration of the intestinal mucous membrane.

Aside from an earthy pale brown discoloration of the skin, syphilis of the liver, so long as no disturbance of the circulation and excretion of bile occur, is not accompanied by any especially dangerous reaction on the general organization, and for this reason the affection frequently lasts for years. It really seems as if the parenchymatous hypertrophy and hyperplasia between the destroyed portions of the liver sufficed for the necessary functioning of the organ (Virchow, Frerichs).

In many cases the kidneys and the spleen are also diseased. The spleen in some cases contains gummatous deposits, more frequently it undergoes an amyloid degeneration similar to the kidneys; enlargement of the spleen and albuminuria as well as the cachexia dependent on these therefore frequently accompany syphilis of the liver. Besides all this, signs of a present or past syphilis found in other organs are of especial importance in the diagnosis.

Diagnosis.

When other symptoms of the constitutional affection are absent in syphilis of the liver the diagnosis between cirrhosis on the one hand and carcinoma on the other may be quite difficult.

An equal distribution of smaller protuberances over the whole surface of the liver and a gradual but continuous reduction in size speak in favor of *cirrhosis*. Protuberances of different sizes, which are unevenly distributed or present only on one or the other lobe of the liver, and conjoined with them an irregular diminution in size of the liver itself or only a part of it, are peculiar to syphilis.

In the differential diagnosis between *carcinoma* and gumma an increase in the growth of the nodules, constant pain, rapid disintegration, loss of strength, the absence of an enlarged spleen and albuminuria, and the somewhat advanced age of the patient will point to cancer, while stationary protuberances, enlargement of the spleen, and albuminous urine point to syphilis. In some cases the diagnosis of the character of the disease is very difficult, and we need not be surprised that gummata of the liver have been extirpated in several cases, being supposed to be cancerous.

The Pancreas.

Disease of the pancreas in the course of acquired syphilis is rare. Rokitansky describes the presence of callosities in other organs than the liver, in individuals affected with constitutional syphilis, and among them, in rare cases, he mentions syphilis of the pancreas; so

also do Lancereaux and Chvostek. Gummata are, however, also found in this organ.

Syphilitic disease of the pancreas may in all probability be difficult to discover during life. Fatty diarrhœa, glycosuria, and epigastric pain occurring in an individual suffering with syphilis are of some value in the diagnosis.

The Peritoneum.

Syphilitic affection of the peritoneum is to be regarded as one of the greatest curiosities. Of more frequent occurrence is a partial involvement of the peritoneum, when organs covered by it become the seat of syphilitic processes, as in hepatic, intestinal, or splenic affections; exceptionally a diffuse purulent peritonitis accompanies ulceration of the small intestine with or without perforation.

SYPHILITIC DISORDERS OF THE RESPIRATORY TRACT.

The Nose.

The beginning of the respiratory tract, viz., the nose and its cavity, is involved quite frequently in the syphilitic process, and the affection of these parts may be observed at each stage of the disease.

Although the *initial lesion* is seen here very infrequently, it has nevertheless been observed upon the tip and alæ of the nose and in its cavity. I have seen it in the shape of a sharply defined, circumscribed, eroded sclerosis involving the lip and nostril in a girl of seven years. The glands at the angle of the jaw and neck were swollen; the buccal cavities contained plaques; and the skin exhibited maculæ. The mode of infection could not be discovered. The initial lesion has likewise been found in the interior of the nose and upon the nasal septum. The submaxillary lymph glands are frequently, the preauricular more rarely, affected.

In regard to the *irritative forms*, we have already remarked in discussing the erythematous and papulocutaneous syphilides that the sulcus of the alæ nasi is by no means seldom the site of desquamating patches or even of moist and ulcerating papules. Moreover, in the first stages a catarrh of the nasal mucous membrane may be observed, though this does not occur very often; just as we see in the mucous membrane of the mouth and pharynx it is produced by a simple erythema or by papules which are localized in these parts. Such a *syphilitic catarrh*—rhinitis catarrhalis syphilitica, erythematosa et papulosa, coryza syphilitica (κόρυζα, a running at the nose)—does not

make itself apparent so much by a tickling sensation and sneezing as by increased secretion and, in the severer forms in which the mucous membrane is infiltrated, especially by a more or less temporary interference with the passage of air through one or both nostrils. It is to be noted that the swelling and secretion are sometimes very slight. The catarrh may even be a "dry" one.

A characteristic of the syphilitic nature of the catarrh is its persistence for weeks and months, and also the presence of erythematous spots and papules of the mucous membrane noted when parts are affected which are accessible to observation.

In addition the secretion of this nasal catarrh contains a considerable admixture of pus corpuscles; indeed, it may be decidedly purulent.

By the decomposition of the secretion, which stagnates in the numerous crevices and recesses of the nasal cavity, foul-smelling masses are produced. On account of the interference with the circulation of air this is usually noticed more by the patient himself than by the examining physician (cacosmia subjectiva).

By no means rarely only a single papule is found in the nasal cavity, and occasionally this grows exuberantly. If a mucous patch ulcerates it will of course increase the accumulation of pus and intensify the other symptoms; moreover, the advancing destruction of syphilitic mucous patches may even give rise to denudation of the thin layers of bones or cartilage which are present here, and finally to their necrosis and exfoliation. But this result is observed rarely, and in most cases we may say that rhinitis syphilitica erythematosa usually leaves no permanent lesions.

Gummata of the nasal integument usually present the same appearance as other cutaneous gummata; and what we have said above of this pathological product, especially of the superficial gummatous syphiloderm, applies equally to gumma of the nose. After persisting for some time the gummatous syphilide of the nose usually leads to destruction not alone of the skin but also of the nasal cartilage. The deformity will vary according to the extent of the loss of substance; the ala nasi is usually destroyed, the process beginning at the border; but I have also observed ulcerative perforation in the middle of the ala. Complete destruction of the whole cartilage of the nose is rare. As a rule small portions alone are actually destroyed while the cicatrized remainder is variously seamed and scarred. Atrophy and shrinking of the alæ of the nose without previous ulceration are more rare.

Disease of the cartilage of the nose as the result of syphilis is indeed of infrequent occurrence; but it is not true, as some authors

state, that its destruction excludes syphilis and should be attributed to another, perhaps lupoid process. Anatomical investigations have also overthrown the general belief that the cartilage is not affected independently in syphilis, but that we have to deal with ulcerative processes which start in the skin or mucous membranes, denude the cartilage, and thus give rise to necrosis. Nevertheless it is true that the cartilage of the nose is not very often affected directly by syphilis, but it is destroyed much more frequently in a passive manner as the result of gummatous processes of the contiguous skin and mucous membranes. Such destruction involves most frequently the cartilaginous septum; the perforation either exists alone or is combined with extensive defects of the nasal bones. Such a perforation, affecting only the cartilaginous septum, often produces no deformity, and is even unaccompanied by any especial distress to the patient (see "perforating ulcer of the cartilaginous septum," p. 133). Its course is sometimes unattended by any symptoms whatever, so that the patient's attention may be first drawn to the defect by the examining physician. On the other hand, the total destruction of the septum mobile produces a repulsive deformity. Both nostrils then coalesce into a single large opening, which is somewhat constricted from above downwards by the dependent tip of the nose, and appears to be drawn out from side to side. If the tip of the nose is also destroyed, then the opening assumes the form of a triangle.

The nasal bones alone of all the bones are imperilled by gummatous processes of the skin; but even deep ulcers of the skin rarely produce denudation or necrosis of these bones. In one of my cases a gummy ulcer of the size of a half-dollar in the roof of the nose on the left side produced necrosis of the underlying bone; and there was a hole as large as a pin in the left nasal bone, through which one could see directly into the nose. Local and general treatment healed the ulcer so perfectly that the cicatrix concealed the opening completely.

In another case there was a large defect in the roof of the nose, together with loss of the nasal bones; the patient relieved the symptoms by closing the opening with a cork. After general treatment I covered in the defect by a plastic operation.

Gummatous affections of the interior of the nose act very differently. Whether the lesion is seated in the mucous membrane alone or in the periosteum and bones, the process leads with extreme frequency, at any rate more frequently than elsewhere, to destruction—*i.e.*, to an ulcer and then to denudation of the bone. This being deprived of its protective covering becomes necrotic, is then loosened from its healthy surroundings by a process of demarcation, and is finally exfoliated. This course is to-day regarded by many clinicians as the

only possible one, though formerly it was generally taught that the frequently very extensive destruction of the bony framework of the nose was produced only secondarily to ulcerative processes of the mucous membrane. Anatomical researches have shown, however, that the nasal bones are also affected by active processes taking place in them, and that the periosteum and bones are very often the primary seat of a gummatous process and are destroyed without participation of the mucous membrane. We have, therefore, to consider gummy processes of mucous membranes and also of the periosteum and bones of the interior of the nose. The general opinion that the nasal cartilage is only laid bare by ulcerative processes of the mucous membrane and of the perichondrium, and is destroyed merely in a passive way is also refuted by the proof of an active affection of these parts.

Rhinitis gummosa, the gummy process inside of the nose, is observed with tolerable frequency and, with few exceptions, only after the disease has existed for a long time. It also continues much longer than the erythematous and papular (simple syphilitic) nasal catarrh, lasting in some cases for months and even years. The serious character of the affections consists especially in the more or less extensive destruction of the nasal structures which it involves.

The first appearance of the gummata is in some cases marked by pains, but ordinarily the initial symptoms are very trivial. The swelling is observed by the patients only after it produces obstruction to the passage of air. Increased secretion occurs usually at an early period. After destruction of the gumma ensues we observe soon an admixture of pus in the secretion and often the mucous secretion is changed entirely into a purulent one.

As the disease advances the purulent secretion constantly increases, inasmuch as the destruction of the bone seldom ceases but usually spreads farther and farther. A part of the purulent secretion, the water of which evaporates rapidly in the air current, dries into a crust, which often coats the walls of the nose extensively. Newly formed pus leads sometimes to a thickening of these crusts, and sometimes to their loosening and removal, so that from time to time large quantities of these discolored crusts are thrown off. This is the reason that the purulent secretion is sometimes very copious and at other times apparently ceases. Another part of the fluid morbid product stagnates and is decomposed, whereby foul-smelling gases are produced. These give rise to cacosmia subjectiva or objectiva, according as they mingle with inspired or expired air.

Necrosis of the bones, which Mauriac observed as early as the seventh month of syphilis, is rarely absent in cases of gumma of the

nose. Whether the gummatous infiltration takes place into the mucous and periosteal lining and produces denudation with consequent necrosis of the bone by ulceration, or whether destruction is produced by a gummatous process originating in the bones themselves, the latter are always very much endangered. In using the probe we very often come in contact with denuded osseous lamellæ. In rare cases these are again covered, but usually they become loosened and exfoliated. It is not uncommon in such cases for patients in blowing the nose or clearing the throat to discharge moderately large pieces of bone besides other products of the disease. If only small pieces of bone are destroyed in this way, the loss does not involve any disagreeable results. If, for instance, parts of the ethmoid bone, a piece or even the whole of a turbinated bone be expelled, it will be no great loss to the patient; even the loss of a not too large piece of the septum does not produce great disturbance, because after the loss of the vomer, for example, the apex of the roof of the nose is sufficiently protected by the intact lamina perpendicularis of the ethmoid bone and the cartilaginous septum. It is only in cases of greater extension of necrosis that we observe notable deformities, because the nose is then deprived of its bony structure. The loss of the perpendicular plate of the ethmoid bone produces sinking of the nasal bones, when the healing process is accompanied by cicatricial contraction.

The bridge of the nose is then bent like a saddle, the tip is tilted upwards, and the plane in which the nostrils are situated approaches the perpendicular. This deformity is frequently observed and indicates unmistakably the process which occurred within the nose. If to this are added partial destruction of the vomer and of the cartilaginous septum with subsequent shrinking of the mucous membrane, we find that the exterior surface of the cartilaginous nares looks as if pushed up beneath the bony part.

When recovery occurs without shrinkage, *i.e.*, with a smooth cicatrix, if the nasal bones are intact, there need be no external deformity of the nose, even if all the other nasal bones are destroyed.

I saw in one case, besides loss of the hard palate and a part of the alveolar process of the superior maxillary bone, gradual exfoliation of the turbinated bones, the vomer, and the whole ethmoid bone; of the septum mobile only the anterior strip of skin which is attached to the upper lip was left; the bridge, the alæ, and the skin of the nose alone were preserved; and yet the nose was not disfigured externally, the only change noticeable to those who knew the man before his illness being that the tip of the nose seemed to be a little nearer the upper lip.

If in addition to the loss of the septum and of the internal nasal

bones the bridge of the nose is also destroyed, then the appearance is as if the skin of the nose, on account of the lack of all bony support, had fallen into the apertura pyriformis; the place of the nose is taken by a few small ridges of skin, which convert the nostrils by constant shrinking into two small round gaps.

In rare cases all the bones of the nose are gradually destroyed, and in such cases we naturally find not only all sorts of deformities but also interference in various ways with the passage of air, and eventually difficulty in breathing and speaking. Sometimes the gummatous process also attacks neighboring parts, as, for example, the nasal process of the superior maxilla, or it spreads to the floor of the nasal cavity, giving rise to necrosis of the horizontal plates of the palatal bones or the palatal process of the superior maxilla, and results in perforation of the hard palate.

The perforation, if sufficiently large, enables us to inspect the structure of the nose from the mouth and to observe readily the processes which develop within its cavity. The patient is further distressed by difficulty in mastication, because parts of the food enter the nose from the mouth. Extension of the affection to the lamina cribrosa is of even more consequence. I have seen meningitis with fatal issue result from such an extension.

The syphilitic process may extend from the nasal cavity into the adjacent sinuses, for example, into the antrum of Highmore, the sphenoidal sinus, and the frontal sinus. The disease seems to extend with special frequency into the frontal sinus, for I have often observed that along with a chronic syphilitic ozæna there are violent pains in the forehead, which can hardly be explained otherwise.

The syphilitic process also extends to the Eustachian tubes, pharynx, and larynx, producing there the changes which we have already mentioned and shall again have occasion to study.

On the other hand a good many disorders of the interior of the nose may be explained by extension of syphilis from the neighboring cavities. In addition to the troubles above mentioned we occasionally observe a diffuse (gummatous) infiltration, especially of the mucoperiosteal membrane. In cases of ulceration the cicatrization is apt to end in extensive adhesions between neighboring parts, usually between the septum and the turbinated bones.

The termination in atrophic contraction and callosities is rarely wanting. A prominent symptom is a very nauseating purulent discharge, which becomes desiccated and converted into dirty, usually adherent crusts.

So long as infiltration prevails the lumen of the nostrils is obstructed, but when shrinking commences, the cavity of the nose be-

comes wider and wider, because in addition to atrophy we find destruction of the bones with mucoperiosteal covering (turbinated bones, etc.).

This process, which lasts sometimes for years, is best described as rhinitis syphilitica atrophica, but it is more commonly called *ozæna* (ὄζειν, to stink) syphilitica; the French, who compare the smell with that arising from a crushed bedbug (punaise) call it "punaisie." It is, however, not uncommon to use the term "ozæna" for other forms of rhinitis, the morbid products of which are also decomposed into stinking masses.

It is characteristic of every form of rhinitis which lasts a long time that the bad odor is not observed by the patient or at least not in the same degree as by those around him (cacosmia objectiva). This phenomenon may be based upon a destruction of the olfactory portion of the mucous membrane or upon the fact that the patient has become accustomed to the especial odor which arises from his nasal cavity; in the first case the perception of a smell is altogether destroyed, that is to say, there is "anosmia." In the second case sensibility to other odoriferous substances will be present.

It must, however, not be overlooked that even when the olfactory function, located in the upper part of the nasal cavity, is preserved, anosmia may be caused by swelling and infiltration of the mucous membrane covering the middle turbinated bones, which result in occlusion of the olfactory fissure (which is situated between the middle turbinated body and the septum). In this case the sense of smell will be restored in a measure, when the diminished swelling of the mucous membrane results in greater permeability of the olfactory fissure.

Diagnosis.

All these processes in the nasal cavity are accompanied by such distinct symptoms that their recognition is attended with no difficulty whatever; moreover, these processes can often be very easily inspected by employing anterior or posterior rhinoscopy according to the location of the disease. Examination of the nasopharyngeal space is very effectively accomplished by introduction of the index finger, bent like a hook, upwards behind the velum.

In those cases, however, in which the disease is located in one of the many recesses of the nasal cavity, we are restricted to the symptoms previously mentioned; denudations of the bones can be recognized in these cases by the probe with little difficulty. Ordinarily syphilitic processes cannot be easily mistaken for other diseases.

Erythematous and papular inflammation of the mucous membrane

of the nasal cavity is rare—perhaps in 1.5 per cent. of all cases of lues—but it is usually associated with other syphilitic affections of skin and mucous membrane, so that the connection cannot easily be overlooked. If, however, other symptoms of syphilis are absent and if a nasal catarrh develops without previous exposure to cold, we shall have to think of a scrofulous origin, and this is especially so if the disease lasts a long time and there is a copious discharge of a mucopurulent secretion. The accompanying or subsequent symptoms, which have been elsewhere discussed, will have to be carefully weighed in such cases.

Syphilitic disorders of the interior of the nose can be mistaken for other affections to an even less extent. There are hardly any other diseases in which the above carefully described destructive processes may occur. In rare cases of *scrofula*, caries or necrosis of one or the other bones of the nasal cavity also occurs, but we find in such cases in addition unmistakable symptoms of general scrofulosis, and these, in connection with the absence of other syphilitic disorders, will usually render recognition easy.

Lupus also extends occasionally from the external nose towards the interior and causes destruction there. In discussing the cutaneous syphilides we have already referred in detail to the differential diagnosis between these and lupus. Inasmuch as lupus of the external integument usually precedes the lupous process in the nasal, buccal, and pharyngeal cavities, a careful examination of the skin will contribute in great measure to an exact recognition of the processes inside of the nasal cavity.

I once saw a case in which lupus had completed its destructive change in the nasal integument, and, moreover, an effort had been made to restore the nose, disfigured by lupous scars, by a plastic operation; this was, however, an entire failure. In such a case when the lupous process attacks the buccal mucous membrane and extends along the hard palate to the velum and the tonsils and there causes moderate infiltration which partially ulcerates, great attention will be required not to confound the existing process with a syphilitic one.

If lupus has been localized from the start in the mucous membrane, we must pay attention to the above-mentioned changes in the buccal cavity.

We must also mention here the *perforating ulcer of the septum* to which Zuckerkandl first drew general attention. This is an ulcerative process in the cartilago quadrangularis which Weichselbaum regarded as diphtheritic. According to M. Hajek's experiments the necrotic process is caused by cocci, viz., staphylococcus pyogenes aureus and streptococcus pyogenes.

The process, which often begins with hemorrhage into the mucous membrane—R. Vottolini indeed calls the ulcer frankly "hemorrhagic"—is in reality a progressive necrosis of the mucous membrane and of the cartilage, and ends with perforation followed by spontaneous recovery, without any especially noticeable participation of the surrounding parts.

According to E. Zuckerkandl the predisposing factor is xanthosis of the septum, which usually develops in the stroma of the mucous membrane after healing and absorption of large extravasations.

Neither mercury nor iodine exerts any influence on the course of this affection, which fact excludes the syphilitic nature of the disorder.

Moreover, it is not associated with other syphilitic symptoms, nor is there any connection with tuberculosis to be found either histologically or bacteriologically, although we often find post mortem tubercles of the lung, sometimes even tubercles of the nasal mucous membrane. However, we find in tuberculous processes foci of granulation which are absent in these cases, as well as infiltration and serration of the border of the ulcer.

By remembering what we have said above, it will usually be possible to recognize the perforating ulcer in the nasal septum as such, and not to confound it with syphilis.

In regard to the differential diagnosis between syphilis and rhinoscleroma and carcinoma we refer to what we have said before.

The Larynx.

The larynx is implicated quite often in the course of syphilis. Most frequently we find *erythema* of the mucous membrane (catarrh) in the early stages of the generalization of the disease—laryngitis syphilitica erythematosa (catarrhalis). Analogous to other mucous membranes the erythematous affection of the larynx appears in various degrees.

Ordinarily there are only redness and infiltration without much secretion; more rarely we find increased secretion with superficial losses of substance (erosions); and also serous infiltration extending to the muscles and of such a degree that paresis is often produced. Between these two extremes we find all degrees of erythema of the mucous membranes. In case of diminished secretion the passing air produces more rapid evaporation of the fluid elements and drying of the secretion into crusts, which adhere to the vocal cords or agglutinate them for short distances. Usually the erythema extends over the whole laryngeal mucous membrane, but we may also see the affec-

tion limited to individual parts, such as the epiglottis, aryepiglottic folds, false vocal cords, etc., or in a general involvement these parts may be especially affected.

The hoarseness varies in degree according to the extent and intensity of the erythema, and indeed it may increase to actual aphonia. The desire to cough and the sensation of dryness will depend upon the amount of secretion.

Syphilitic erythema of the larynx is often one of the first symptoms of general syphilis and is accompanied by similar affections of the palate and pharynx; by mucous patches in the mouth and by the first eruptions on the skin. Sometimes it disappears before the other symptoms, sometimes it lasts much longer than the others. Patients who as a result of their vocation are exposed to the inclemency of the weather, do not recover from the erythema for a long time, as they are more subject than others to relapses during the first and second year.

A *papular eruption* in the larynx—laryngitis syphilitica papulosa—is perhaps much rarer, occurring in two to three per cent. of all syphilitic persons. The papules appear as infiltrations of the size of a lentil or larger, elongated rather than round, or even cylindrical (on the vocal cords). They project very little above the general surface. They often look as if coated with a grayish-white epithelial scurf, or, after this falls off, the surface exhibits a red punctate appearance or it may even be ulcerated. Their most frequent site is the free border of the epiglottis, whence they usually extend towards the posterior surface; also the aryepiglottic folds and the mucous membrane over the arytenoid cartilage. They are observed more rarely on the true vocal cords; the papules are not infrequently surrounded by ordinary erythema.

The symptoms caused by the papules are often not more important than those of erythema, but when the papules are situated in the interarytenoid region there are apt to be painful fissures.

Intense swelling of the true and false vocal cords has been observed several times when the primary infection occurred in the neighborhood, as upon the lips, for example. In a case reported by Armand Desprès a proliferating mucous patch on the right vocal cord caused such severe dyspnœa that tracheotomy had to be performed. The papular affection usually coincides with the first eruptions and is associated with them. It undergoes resolution much more rapidly than erythema; a *restitutio ad integrum*, even after breaking down of the mucous patch, is the usual result.

At a later period *gummata* also form in the larynx. They appear either in the shape of many small nodules or as diffuse infiltrations.

The epiglottis, the aryepiglottic folds, the posterior surface of the arytenoid region, and the true and the false vocal cords are often the seats of gummatous disorders. These cause, according to their situation, various deformities of the epiglottis, shapeless thickening of the aryepiglottic fold, the false vocal cords, and the arytenoid cartilage, or protuberances on the true vocal cords. The latter may assume a gelatinous aspect when the infiltration is uniform (L. v. Schrötter).

In connection with these changes we find difficulties of phonation, and, if there is considerable infiltration of both vocal cords, notable stenosis of the glottis.

At the outset the gummata are covered by a dark red mucous membrane which pales gradually as the absorption of the infiltrate progresses. On the whole, however, they are absorbed more slowly than in other places, especially the larger gummy nodes, which are, however, rarely met with in these parts. Frequently the gummata break down and ulcers then form, the edges of which are infiltrated, sharply cut, sometimes as if punched out. The floor of the ulcer is coated or red and granulating, according as necrotic particles are still adherent or not. Occasionally papillomatous proliferations are found on the floor and border of the ulcers. These usually persist even after cicatrization of the ulcer, and probably have no connection with syphilis as such.

Concerning gummatous affections of the laryngeal muscles we possess few authentic observations. In other parts the destruction caused by gummata is often very extensive. On the epiglottis they soon cause denudation of the cartilage, which rarely acquires another covering and usually becomes necrotic. In this manner the epiglottis may ulcerate in great part or entirely, or the gummy process may entail destruction of the other cartilages.

The occurrence of perichondritis will produce separation of the cartilages, which usually become necrotic, partially or wholly. Gummy processes which affect the perichondrium and cartilages from the beginning are rarer. In either case an abscess forms around the necrotic cartilage, or an ulcerated cavity which exposes to the danger of suffocation as a result of its extension, or of the development of œdema. In cases with good results the sequestra become loosened and are expectorated during a coughing spell.

Türck, Lewin, Karl Störk, L. v. Schrötter, and others report such observations.

If gummata of the true vocal cords undergo ulceration, they appear here and there as if eroded on the free border, or are detached on the posterior border from their insertion into the processus vocalis. If the ulcer is situated in the angle between epiglottis and pharyngo-

epiglottic arch, on the posterior surface of the larynx, or on some other part which is concerned in deglutition or is moved during speaking or respiration, the pains are often very severe, especially during these physiological acts. Disorders occur also when in case of defect of the epiglottis or as the result of imperfect action of the laryngeal muscles, fluids or particles of food enter the larynx, or speech is impaired by ulcers of the vocal cords. In rare cases syphilitic affection of the larynx causes severe spasm of the glottis, to which the patients succumb, if not saved by tracheotomy, or œdema of the glottis complicates syphilitic laryngitis and necessitates tracheotomy. A syphilitic ulcer in the larynx may also terminate fatally as the result of hemorrhages (Ludwig Türck). At other times we see the remains of syphilitic ulcers persisting for years, without special annoyance to the patients.

According to the location and extent of the loss of substance cicatrization produces all kinds of disorders. Small ulcers in indifferent places may heal completely and leave behind them no trace of their existence. The vocal cords are, it is true, very sensitive in this regard, because very small cicatrices impair normal intonation. One might suppose that even after cicatrization of larger losses of the epiglottis a deficient closure of the larynx during eating and drinking would remain permanently, but this is not the case. Even complete loss of the epiglottis does not have this effect, for patients learn to contract the laryngeal muscles so as to close the aperture during the act of deglutition.

In the interior of the larynx we occasionally see bands of adhesions stretching from one to the other side during the process of cicatrization. This cicatrization may prove very serious if it occurs in ulcers of both vocal cords simultaneously, thus inducing synechia. The adhesion begins usually at the anterior angle and seems to progress quite rapidly. The posterior angle remains usually open in the form of a larger or smaller, round or sickle-shaped gap. Below the vocal cords adhesions like a diaphragm have also been known to obstruct the laryngeal space.

Adhesions of the epiglottis to the arytenoepiglottic ligaments and to the arytenoid cartilage have also been observed. It is self-evident that the difficulty in breathing must increase with the increasing narrowness of the opening left over after cicatrization, and that in some cases this dyspnœa may increase to such an extent as to threaten suffocation and may render an operation necessary. Œdema of the glottis will be very dangerous if complicated with stenosis of the larynx; in such cases tracheotomy becomes inevitable.

How large the aperture remaining between the vocal cords must

be to permit of respiration it is not easy to say. In some cases apparently large openings cause serious suffocative attacks, while in other cases much smaller gaps are well tolerated. It is possible that the rapidity of development of the stenosis is an important factor, because the patient may become accustomed to a slowly developing stenosis of the larynx. Under such conditions impairment of the voice is probably always present.

By no means infrequently we see, in addition to these ulcerative affections of the larynx, similar conditions in the neighborhood, and in such cases, of course, there is a possibility of adhesions to other parts. Once I saw the upper surface of the epiglottis in its left half adherent to the tongue by cicatricial tissue, but in spite of the impossibility of closing the entrance of the larynx deglutition was effected without difficulty. If ulcers occur simultaneously in the epiglottis and the pharynx there will be the danger of serious dysphagia and dyspnœa resulting from the formation of adhesions between the rim of the epiglottis and the walls of the pharynx.

Diagnosis.

In cases of laryngeal trouble such as we have described, we must never fail to examine for evidences of present or past syphilitic lesions in the pharynx, mouth, or nasal cavity, on the general integument, in the osseous system, or in the testicles. Laryngitis erythematosa in particular cannot be recognized as syphilitic except in connection with the general symptoms of constitutional syphilis. The recognition of laryngitis papulosa is less difficult, because the bluish-white, sometimes eroded or ulcerated patches are quite characteristic of syphilis. In laryngitis gummosa and ulcerosa we shall succeed in making a diagnosis most readily by noting the other changes in the larynx, and also by means of exclusion.

The practitioner is called upon most frequently to differentiate *tuberculosis* from syphilis of the larynx. Unlike the syphilitic, tuberculous ulcers are not seen upon a red and infiltrated base, but occasionally we find hemorrhagic suffusion of the laryngeal mucous membrane, and very often the edges and floor of the ulcers are pale and the whole larynx is anæmic. Furthermore, tuberculous ulcers are not so deep, nor do they produce such extensive destruction and rarely necrosis of the cartilage. Altogether they are remarkable for their insidious course and slight tendency to healing. As in the pharynx and upon the tongue here also yellowish nodules in the surrounding parts indicate tuberculosis with a considerable degree of certainty. Moreover, the existence of tubercles in other organs, especially in the

lungs, is very important in the differential diagnosis. Further, we have to consider that the appearance of the patient may be a very healthy one in syphilis, but not in tuberculosis. Absolutely decisive is the actual discovery of tubercle bacilli. It is advisable to collect the secretion from a suspicious ulcer in the larynx on a small sponge or pledget of sterilized cotton and submit it to a bacteriological examination.

An isolated *scleroma* in the larynx is difficult to recognize, but the diagnosis would be established by the finding of characteristic rhinoscleroma bacilli in excised particles. The diagnosis is easier if rhinoscleroma is found at the same time in the nose and in other sites of predilection. Sometimes the difficulties increase to such an extent that, at least in the beginning, the diagnosis must be regarded as doubtful. This is especially true when the affection is limited to the larynx and the other pathological symptoms are slight, or when an undoubtedly tuberculous individual becomes syphilitic, or when tuberculosis subsequently complicates syphilis. The true nature of the disease cannot always be determined in such cases, even ex juvantibus, because antisyphilitic therapy in this combination of both diseases either has an effect only at the beginning or is not tolerated at all.

Equally difficult may be the condition if we are forced to decide between *carcinoma* and syphilis. The condition of the adjacent lymphatic glands is not always of assistance in such cases, because swelling of these glands may be left over from former attacks. Even long-continued observation may fail us at times.

Laryngeal carcinoma, which usually ulcerates at an early period, may be easily mistaken for ulcerating gummy nodules. More rapid destruction, great tenderness and swelling of the neighboring lymphatic glands, which had not been enlarged before, and the absence of other syphilitic symptoms will indicate carcinoma.

Lupus, *leprosy*, or *glanders* usually develops in the larynx only after the disease has existed for some time elsewhere; therefore we almost always find corresponding changes in skin, etc.

The Trachea and Bronchi.

Syphilis is rarely localized below the larynx, but certain changes have been observed here belonging to one or another of the stages of syphilis.

Seidel has reported a case in which there was a large papule on the posterior wall of the trachea, which disappeared under mercurial treatment. Mackenzie saw similar lesions of the trachea in five cases. It is not unlikely that some cases of bronchial catarrh in the first

stage of syphilis may be due to irritative syphilitic processes in the trachea and bronchi, similar to those that occur on the soft palate, in the pharynx, and in the larynx. According to Mackenzie even such apparently mild cases must be regarded as serious.

More frequent are well-authenticated observations of grave tracheal affections which are to be regarded in great part as due to the presence of gummata or their remains. Circumscribed gummy nodules do not seem to be so frequent in this region as diffuse gummy infiltrations. Ulceration, sometimes resulting in denudation of the cartilages, is the usual termination. In the latter event the cartilages become necrotic, in connection with a tracheal perichondritis, and are either expectorated or are simply destroyed. Sometimes the cartilages become ossified.

In a case reported by F. Moissenet many cartilaginous rings were destroyed, and only eleven or twelve could be counted. In some cases the gummy process has extended to the connective tissue surrounding the trachea—peritracheitis syphilitica. Occasionally the gummy process extends to other important parts in the vicinity, such as the aorta, pulmonary artery, and œsophagus, and involves them in destruction.

In a very instructive article by C. Gerhardt, we learn concerning the chief localization of syphilitic affections of the trachea that in four out of twenty-two observations the whole wall of the trachea was affected, in six the upper portion, in twelve the lower half, usually in the neighborhood of the bifurcation. The larynx also appeared to be affected in most of the cases in which the disease extended over the greater part of the trachea or even over its upper half. There was also, but not so regularly, a concomitant affection of the bronchi whenever the whole trachea or its lower half was diseased. The issue in such cases, according to Gerhardt, is usually fatal. Alfred Rey and Anton Vierling have come to similar conclusions as the result of their studies. Of independent syphilitic disorders of the trachea and bronchi, without participation of the larynx and the pharynx, we possess few observations.

In individual cases the course of tracheal syphilis is favorable in so far as the necrotic parts are cast off, the infiltrations are absorbed, and the ulcerations heal. At the same time many kinds of deformity of the trachea are produced. If entire rings of cartilage are destroyed, there results at least a shortening of the trachea (Moissenet); if the ulceration affects only one side of the rings, they may be twisted and bent; and furthermore, such deformities are usually combined with narrowing of the lumen.

Stenosis of the trachea may occur also without the previous occurrence of any cartilaginous affection. Either there are more or less

firm, circumscribed infiltrations projecting into the lumen of the trachea; or there may be a diffuse infiltration causing a stenosis of the tube in its entire extent; or there are diaphragm-like partitions which sometimes look as if composed of concentric rings, narrowing the trachea from above downwards; or finally there are cicatricial cords running from side to side, forming a sort of trelliswork. The occlusion of these meshes by mucus produces apnœa, although only temporarily. Above and below the stenosis we find the trachea evenly dilated. Tracheal syphilis, especially if it extends over a large part of the mucous membrane and if ulceration is present, is accompanied by increased mucopurulent secretion, by râles, and a tickling sensation which gives rise to cough; sometimes also there may be pain located behind the sternum. At the same time there is found in varying degree, according to the swelling and infiltration, a narrowing of the trachea which produces dyspnœa. While the process is still in its florid stage the symptoms will vary as a result of increasing or decreasing infiltration, of extensive collapse, and of necrosis of the tracheal cartilages, which are expectorated in small or large pieces. In the latter case dangerous attacks of suffocation are rarely absent. A fatal issue also results from an extension of the disease to the bronchi; from perforation of tracheal gummata into the mediastinum or into the surrounding connective tissue, sometimes attended by the development of ichorous foci. In cases in which the tracheal gummata penetrate into the œsophagus death is due to "foreign-body pneumonia." Fatal hemorrhages have also been reported as the result of an extension of syphilitic ulcerations of the right bronchus to the pulmonary artery or one of its branches; also after perforation by a gumma of the trachea into the arch of the aorta or the vena cava. But the stenosis produced by the disease is alone capable of producing a fatal issue.

Some patients survive even grave forms of tracheal syphilis, for example, involving a loss of a large number of cartilaginous rings, but they suffer afterwards from the results of the cicatricial stenosis. We observe the peculiarity that stenosis extending over a large area of the trachea causes important disorders, even if the lumen does not appear much diminished, while much more marked stenoses, if they are shorter, are tolerated much better. In course of time the cicatrix narrows the lumen more and more, and diminishes the supply of air, and this, in many cases, is followed by pneumonia or pulmonary œdema. To these diseases the patients usually succumb, if they do not die earlier from apnœa.

The disease of the trachea is easily recognized from the symptoms above enumerated. With the help of the laryngoscope we may often

ascertain the form of the morbid process, but the determination of its exact location is attended with optical difficulties.

When stenosis of the trachea is present, dyspnœa, especially inspiratory dyspnœa, is evident; speech is not necessarily affected, apart from diminished volume of the sound. Tracheal stenosis develops generally slowly and is not, like stenosis of the larynx, usually combined with dysphagia and local tenderness. According to Gerhardt, much less extensive excursions of the larynx during respiration are observed than in laryngeal stenosis. If the stenosis affects only one principal bronchus, we are likely to find weakened or deficient respiratory murmurs with normal percussion sound in the pulmonary area supplied by this bronchus, but stenosis of both bronchi produces the same results as tracheal stenosis.

Accompanying affections of the larynx, the nose, and other parts will aid considerably in the diagnosis. The ulcers of glanders, which have the greatest resemblance to syphilis, are rarely observed in this location; moreover, the histories of the two cases are very unlike. If there is a cicatricial stenosis we may diagnose syphilis in the great majority of cases.

Störk observed in some patients a chronic blennorrhœa which affected the nasal cavity and also the laryngeal and tracheal mucous membrane. This disease, which has absolutely no connection with syphilis, produces thickening and other severe changes of the mucous membrane, which finally extend also to the trachea. The clinical observations of Störk have been abundantly confirmed by Koehler, Semon, Chr. Lemcke, and others. But there is now no longer any doubt concerning the nature of this affection, inasmuch as v. Schroetter's assertion that the process is "identical or similar to rhinoscleroma" has been amply confirmed by later investigators (Chr. Lemcke). The possibility of an independent affection of the trachea as well as of the larynx by rhinoscleroma (preferably called scleroma by Ganghofner) can no longer be doubted, and this is a fact which has to be considered in cases of a difficult diagnosis.

Pulmonary Syphilis.

Besides some allusions of earlier writers on syphilis (Peter Pinctor, Paracelsus), we find in the works of famous physicians of former centuries undeniable observations of pulmonary affections resulting from syphilis. The first observations of undoubted pulmonary syphilis were made by Ricord, Lebert, Dittrich, Vidal, Hecker, Wilks, Virchow, Wagner, Foerster, Lancereaux, H. Ramdohr, A. Sokolowski, and others, and these were followed by other observations in a con-

tinuous series up to the present time. A. Hiller has collected more than half a hundred well-authenticated cases which he critically examines in his excellent work.

Pathological Anatomy.

Most characteristic of pulmonary syphilis is the anatomical demonstration of gummy nodules. These are rarely single, but though multiple are found as a rule more often on one side than on both sides. The middle and lower lobes are probably more frequently affected, but we also find gummy deposits at the apex. The nodules, which usually vary from the size of a pea to that of a walnut, seldom larger, are rounded, often also serrated, and provided with long projections; they are grayish-red on section, and dry or yellowish and soft in the centre. The intervening pulmonary tissue is infiltrated or shrunken. According to Virchow a multiple, chronic, indurated pleuropneumonia or bronchopneumonia develops therefrom. This produces either on the surface of the organ, upon and immediately beneath the pleura, or around the medium-sized and smaller bronchi, very firm, callous foci, which have mostly a cicatricial character on the surface of the lung, a tubercular or even nodular character in the interior of the organs. They are hard to the feel, are cut with difficulty, and consist of very firm, occasionally even sclerotic connective tissue.

The latter is white *per se*, but often assumes a spotted bluish-gray or almost purely black aspect as the result of the absorption of carbon pigment. Such foci may even attain the size of a walnut, and if many are situated close together, a large part of the lung may become impermeable and the patient will be asthmatic.

The hyperplasia of the connective tissue is conspicuous here; it starts chiefly from the walls of small or larger bronchi—therefore at the hilus of the lung—or from the adventitia of the pulmonary vessels. The bronchial tubes often participate in the syphilitic process. In such cases we find stenosis of the tubes; frequently there are also bronchiectatic cavities, which form about the stricture or in the smallest bronchi below the cicatricial contraction.

Pulmonary syphilis has also been shown to exist in the form of a diffuse infiltration in one or both lungs or in single lobes. In these cases the pulmonary tissue is firm, devoid of air, homogeneous, of a dirty yellow or dirty red color, or pale—the "white hepatization of the lungs" as seen in hereditary syphilis. The starting-point of the infiltration is the interstitial connective tissue and the walls of the arteries and bronchi. As a result of further shrinking the alveoli become constricted and are filled with desquamated epithelium.

In adults there is a second form, similar to catarrhal pneumonia, in which the entire pulmonary lobe appears firm, devoid of air, pale or reddish gray, and on the section presents a peculiar gelatinous appearance.

The local disorders, which occur more frequently in adults, may also be associated with the diffuse infiltration which is found more often in the new-born. In such cases the parts between the gummata not rarely show diffuse syphilitic infiltration in the same way that the diffuse syphilitic pulmonary lesions often contain in their midst or at the periphery gummy nodules, which are usually miliary in character; or there may be other combinations of lesions.

Symptoms.

According to the most recent researches there seems to be no doubt that the lungs become affected, usually in a catarrhal form, very soon after the syphilitic infection. I have observed in several cases of primary or relapsing roseola symptoms of a pulmonary catarrh which disappeared with the syphilide or lasted a little longer than the latter. Although there are no characteristic symptoms which would show such a catarrh to be syphilitic, the accompanying symptoms and the ordinarily protracted course allow of a probable diagnosis. Grave pulmonary disorders have also been observed at this stage.

Most observations of pulmonary syphilis, however, have been made in patients who had suffered from syphilis for some time, usually for several years.

The patients complain first of difficult respiration, which becomes more severe after fatiguing movements or in case of an ordinary catarrh supervening as a complication, and ends in actual dyspnœa. Soon cough occurs with scanty expectoration and slight pain. These symptoms, which are usually worse in the evening, may exist for some time without provoking a change in the otherwise blooming appearance of the patient. Indigestion is rarely complained of, and there is usually no fever.

In this stage we find in the diseased part of the lung either very trivial changes in the physical signs or a dull percussion sound and weakened respiration, or increased bronchial inspiration and hardly any expiration. The more pronounced the latter conditions, the more conspicuous is the impairment of the respiratory movements of the thorax. With the progress of the affection all these symptoms increase, or we observe with increasing destruction symptoms of the formation of cavities. Dyspnœa, pain, and cough increase, expec-

toration becomes copious and purulent. Hæmoptysis is rare, but profuse bleeding has been observed in some cases. Now the strength of the patient begins to wane, appetite decreases, fever sets in. Cachexia and collapse complete the picture of a pulmonary phthisis.

The new-born usually succumb quickly to a syphilitic pulmonary disorder. If the interstitial form of the syphilitic pulmonary disease is little developed at birth, the children may survive. In adults the course is generally milder. On account of the slight fever accompanying syphilitic pneumonia or gummy nodules, the patients do not lose their strength so rapidly, and they preserve for a long time, in spite of their extended pulmonary disorder, a tolerable appearance. Even advanced pulmonary affections with widely extended infiltrations and destructions permit the hope of a cure by antisyphilitic treatment.

A peculiarity of these specific pulmonary disorders is the fact that the objective and subjective symptoms are not always proportionate. Sometimes the physical examination indicates an extensive disorder while the patient feels comparatively well. In other cases there is severe dyspnœa, the cause of which is not explained by the results of the physical examination. The asthma is due to compression of the bronchi by enlarged glands and infiltrations, or a stenosis due to contracting cicatrices, or it is due to aortic endarteritis (asthma cardiacum).

Diagnosis.

The syphilitic process is located most frequently in the middle parts of the lung, especially on the right side. Accordingly the physical symptoms are most clear above and below the clavicle, between the shoulder blades, or in the region of the angle of the scapula on the right side. Sometimes the onesidedness of the process or the escape of the apex is mentioned as characteristic of syphilis. But there is no doubt that the apices of the lungs may also be affected in syphilis. The nature of the disease of the lungs is especially indicated by symptoms of syphilis in other parts, such as fresh syphilitic products or characteristic ulcers in the skin, the subcutaneous tissue, or the bones; perforations and defects in the nasopharyngeal or buccal cavity; fresh or old syphilitic processes in the nervous system or the organs of special sense; and other specific lesions, especially the presence of ulcers in the larynx or trachea.

The accompanying syphilitic symptoms are, however, sometimes very trivial or easily overlooked. The less characteristic these are of syphilis, the more difficult it will be to make a differential diagnosis from *tuberculous disease*. A sharply circumscribed dulness in

the middle of the lung should always arouse suspicion of syphilis, which will be increased if the patient does not belong to a tuberculous family, has no tuberculous habitus, and appears well nourished. Under all circumstances the sputum should be examined repeatedly for tubercle bacilli.

If tuberculosis and syphilis exist together, the diagnosis is of course difficult, whether it be that a tuberculous person is infected with syphilis or—what surely happens occasionally—a syphilitic person becomes tuberculous.

Syphilis of the Pleura.

Independent of the lungs the pleura seems to become affected only exceptionally; but an affection of this serous membrane, especially in its pulmonary part, is not rare as an accompaniment of pulmonary syphilis.

SYPHILIS OF THE CIRCULATORY SYSTEM.

The Heart.

Affections of the heart in the course of lues are recorded by the most ancient writers on syphilis, but they considered them due to the use of mercury. Lancisi described cases of aneurysm of the heart and Morgagni observed alterations in the heart and in the pericardium repeatedly at autopsies of persons dead of syphilis. The first observations in recent times on disorders of the heart in syphilis were published by Ricord, Lebert, Virchow, and Wagner. Before that time such affections appear to have been considered as tuberculosis of the heart (Virchow).

Gummata of the heart have been observed repeatedly; they occur in all muscular parts of the heart, in the walls of the ventricles and auricles, in the septum, and in the papillary muscles. In the septum they seem to become more voluminous, forming there nodules of such size that they protrude into both ventricles.

There is furthermore a simple fibrous syphilitic myocarditis with multiple fibrous cicatrices in the heart muscle. In fibrous syphilitic myocarditis partial aneurysms of the heart have been repeatedly observed. Fibrous as well as gummy myocarditis is usually associated with a sclerosing endocarditis or with partial pericarditis. Independent syphilitic disorder of the pericardium without disease of the heart muscle has rarely been seen.

Endocarditis may attack merely the lining of the myocardium, and extends in such cases over a small area; or it may attack the

valves, in which case the process extends usually from the vicinity of the valves to their insertions. The valves are then thickened or appear as if pushed aside by the gummata. In such cases we observe symptoms either of insufficiency or of stenosis. The symptoms of valvular deficiencies may also be produced by extension of the fibrous or gummy myocarditic process to the papillary muscles, and their consequent shortening. Independent syphilitic disorders of the free borders of the valves are very rare. Endocarditis syphilitica of the coronary arteries has also been observed, also disease of the blood-vessels of the heart generally, as a result of which hypertrophy of the heart may occur (Chvostek). In a case reported by Paul Palma syphilitic disease of a branch of the left coronary artery was the occasion of an aneurysm of the heart.

Symptoms.

It is conceivable that the heart may be attacked even during an early period of syphilis and that the transient palpitations and dyspnœic conditions from which some patients suffer may be connected with the generalization of the disease. At all events it is permissible to connect such symptoms with the chloræmia of beginning syphilis.

According to our experiences thus far, however, we must hold that the syphilitic process is localized in the heart only after the disease has existed for several years. The symptoms are the same as in chronic myocarditis. Very often the morbid change develops without any special symptoms. The majority of patients die suddenly and the autopsy reveals cardiac syphilis as the cause of death. Sometimes the patients complain of general weakness, palpitations of the heart and precordial pains; often they are attacked by a sensation of fear and oppression on the chest and later by pronounced dyspnœa.

Physical examination results either negatively or we find somewhat increased cardiac dulness; the heart sounds are also sometimes normal, sometimes muffled and weakened or accompanied by a slight blowing murmur; the contractions of the heart are often weak and unequal, and the pulse is correspondingly small and irregular. The general integument, especially of the face and extremities, is pale and cyanotic, or there are signs of threatening gangrene in peripheral parts; œdema and dropsy develop; the urine contains albumin; signs of valvular deficiency are rarely present, but have been observed occasionally.

Diagnosis.

The diagnosis of cardiac syphilis must be based upon the history of the case and the existence of clearly pronounced syphilitic symptoms in other organs; but we must not forget that sometimes these symptoms may be absent.

Prognosis.

The course of cardiac syphilis is in most cases an unfavorable one, and the cause of death varies as in myocarditis generally. But there are some cases reported with favorable issue. It is probable that the possibility of recovery or improvement in such cases depends upon the stage of the disease at which treatment is begun.

The Blood-Vessels.

Clinical and anatomical observations of syphilitic affections of the larger arteries date far back. The occurrence of syphilitic disease of the smaller blood-vessels did not escape the observation of Morgagni, but it is only of recent years that syphilitic disorders of the blood-vessels have been fully recognized. Attention was then drawn anew to the changes in the blood-vessels which were often found with other symptoms of lues, and which were not rarely directly caused by syphilis.

In recent times clinical observations have been made which justify the assumption that aneurysms are directly produced by syphilis.

Thus Lancereaux saw an aneurysm of the subclavian artery improve under the administration of potassium iodide. A. Hertz noted an etiological relation between syphilis and a sacculated aneurysm of the descending aorta in a woman, thirty-four years of age, who had been infected two years previously. G. W. M. McNalty observed in a soldier, thirty-five years old, who had been infected five years before, an aneurysm of the aorta, forming a tumor, two and one-fourth inches broad and three-fourths of an inch high, which protruded under the right sternoclavicular articulation, and became smaller and firmer under the use of potassium iodide; a few months later there was an ulcer on the outer side of the left knee-joint, the former condition became worse again, and the patient died. At the autopsy numerous gummata were found in the heart, and in the endocardium the aortic valves were thickened, and on one of them was a bone-like deposit; the other valves were normal. The innominate artery and a portion of the ascending portion of the arch of the aorta were converted into aneurysms, which constricted the trachea and had de-

stroyed the manubrium sterni and the cartilages of the first and second ribs.

Langenbeck demonstrated in a case of aneurysm of the ascending aorta, in four cases of aneurysm of the aortic arch, and in about half of all the aortic aneurysms which he had seen that the patients had suffered for some time from syphilis. The frequently conspicuously favorable effect of potassium iodide in the treatment of aneurysms is perhaps to be explained by this fact.

Jaccoud reports a case of a fifty-year-old woman who presented symptoms of syphilis and suffered from an aneurysm of the aorta; each time that treatment with potassium iodide was instituted the condition markedly improved.

Arteritis of the abdominal aorta of syphilitic origin (as I believe) was observed by me in a man of thirty-two years. The patient had been infected three years before and since had suffered repeatedly from attacks of gummata and gummy ulcerations; during the last few weeks he had suffered from violent abdominal neuralgia, which tormented him day and night and for which he was treated unsuccessfully. When he called on me I discovered, besides numerous cicatrices of ulcers and bilateral syphilitic orchitis, a broad, pulsating, extremely sensitive tumor upon the lumbar spine. The tumor also appeared to extend to the left towards the renal artery; it was evident that this was due to an arteritis (aneurysmal enlargement of the abdominal artery). My colleague, M. Heitler, who examined the case uninfluenced by me, noted the same condition. Treatment with potassium iodide relieved the pains to a notable degree after other remedies had failed entirely. W. C. Maclean believes that syphilis, at least in soldiers, is a frequent cause of aneurysm. Other authors also are agreed in regard to the connection of aneurysm and syphilis. In July, 1876, Francis H. Welch made a series of exhaustive investigations among soldiers and found undoubted syphilis in seventeen out of thirty-four cases of aneurysm, and probable syphilis in eight cases. Among fifty-six fatal cases of syphilis he found disease of the aorta in sixty per cent. Vallin, Verdié, Karl Malmsten, Senator, and Ewald also dwell upon the importance of syphilis in the etiology of aortic aneurysms.

Concerning aneurysms of the cerebral arteries, the rupture of which often produces death, we have reports of a number of instances. Affections due to syphilis have also been found in larger arteries, which are easily accessible to palpation. M. Zeissl has described a case of arteritis of the left brachial artery.

Some years ago I saw a case of syphilitic arteritis of the popliteal

artery in a man of 32 years who was infected when 19 years old, and had been under treatment for syphilis a number of times in different hospitals (two and one-half years previously he had been in my ward). Beside fresh gummy tumors and numerous cicatrices of former lesions on the whole body, we found in the left popliteal space a distinct prominence. This was produced by a tumor, corresponding to the popliteal artery, elastic, cylindrical, with a diameter in the middle of 4 cm. and disappearing above and below beneath the muscles. The tumor showed distinct pulsation posteriorly and laterally. The arteriæ dorsales pedis and the tibiales posticæ pulsated synchronously; but the pulsation of the tibialis postica of the left side appeared a little weaker. The patient felt weakness and slight pains in the left leg. There were no differences in sensation. Six days after treatment was begun (which consisted of potassium iodide internally and mercurial plaster externally) there was a notable reduction in size of the popliteal tumor and also a perceptible diminution of the pulsation. After about four months the patient left the hospital considerably improved.

James O'Grady reports a case of popliteal aneurysm in a man of twenty-eight years, who had previously acquired syphilis. Heyberg also reports a popliteal aneurysm in the eleventh year of syphilis, in combination with aneurysms of the aorta and innominate artery. Arteritis syphilitica is further important, inasmuch as by constriction of the lumen of the artery the blood supply is cut off from the peripheral parts. The latter then become cold, livid, insensitive, and finally gangrenous. Many cases which have been described as Raynaud's disease may have been caused by such a syphilitic arteritis which had produced impermeability of the vessels.

Special importance attaches to syphilitic affections of the medium-sized and smaller arteries. According to the investigations of recent years these occur quite often in the brain and also in other organs. The most extensive investigations in this regard were made by O. Heubner, and refer to the arteries of the brain. The vessels gradually lose their red color, and become grayish-white; their flattened cylindrical shape becomes at the same time round; their consistence grows firmer and even of cartilaginous hardness. On section the lumen appears diminished by thickening which starts sometimes from one side, sometimes from the entire periphery; the non-stenosed portion of the artery is either obstructed by a thrombus or the artery is completely obliterated.

According to Heubner the new growth, whose principal seat is between the membrana fenestrata and the endothelium, originates usually from proliferated endothelia. These form a firm connective tissue composed of spindle and stellate cells, into which later round cells immigrate from the vasa vasorum. The proliferation assumes

thereby the character of a gumma (syphiloma) and produces during its course cicatricial changes in the arterial walls. Above the diseased parts aneurysmal dilatations are not infrequently found. The process continues also along the artery and thus leads to atrophy of large vascular territories.

These investigations were confirmed later not only for the cerebral vessels, but also for many other territories.

Syphilitic affections of the *veins* have also been observed several times. Langenbeck extirpated a tumor on the right side of the neck which he took for a carcinoma. Microscopical examination as well as later the occurrence of ulcerative processes on the tongue and the left pharyngeal wall and the left cheek proved the gummy nature of the tumor; it probably had started from the external wall of the jugularis communis. In another case the gumma, which had been taken for a malignant tumor and was extirpated, started from the femoral vein or the surrounding connective tissue. Here, too, the internal walls of the vein were degenerated and brittle, and a firmly adherent discolored thrombus was found in the lumen of the vessel; the thrombus had a fresh appearance only in the central part. Phlebitis of the superficial veins of both legs and gummata of the muscles were observed by E. H. Greenhow in the case of a merchant, thirty-three years of age. The veins had been converted into painful cords; the extremities were swollen and painful to the touch; the inguinal glands were swollen. The administration of potassium iodide soon gave relief.

A case of bilateral phlebitis of the vena saphena and periphlebitis of the right side was seen by me in the person of a patient at my clinic, a man, 26 years old, who had gone through a mercurial treatment on account of an initial sclerosis and a macular syphilide. There existed, besides mucous patches, recurrent roseola and psoriasis palmaris. Upon the inner surfaces of the legs and thighs, starting from the internal malleolus on each side, was found a firm cord, nodular in places and as thick as a goose quill. It could be traced under the skin up to the fossa ovalis. Upon the right thigh it was swollen and formed a hard protuberance, the thickness of the thumb. The surrounding cellular tissue was, moreover, infiltrated and the skin was red and protruding in the form of a longitudinal tumor. Examination was painful; the process had lasted only a few days. As there was no œdema, we had to assume the existence of free anastomoses with the deeper veins. The patient was ordered to take calomel and to apply emplastrum cinereum on the hard cords; at the end of three months there was no trace of the tumor to be seen.

A. Breda reports two cases of phlebitis syphilitica; in one the left crural, cephalic, basilic, and median veins were affected; in the

other the veins of the left leg were attacked. Both patients were quickly cured by antisyphilitic treatment.

Charcot also reports two cases of disease of the saphena vein which disappeared gradually under appropriate treatment.

Symptoms.

The symptoms connected with syphilitic affections of the vessels naturally differ greatly and depend upon the location and extent of the disease, upon the size of the affected vessels, and in the case of smaller vessels upon the importance of the organ whose circulatory region is the seat of the pathological process. The usual result of the changes above described is that the walls of the blood-vessels lose their elasticity partially, or become considerably thickened. Hence there is sometimes enlargement, at other times narrowing and obliteration of the lumen of the vessel. Although both results may occur together, enlargement affects more often the larger vessels, narrowing of the lumen more frequently the medium-sized and smaller arteries. Accordingly we have to expect in the course of the process in the arteries sometimes the formation of an aneurysm, sometimes the symptoms resulting from obliteration of the vessels. Arteritis resulting in narrowing and obliteration will be less striking, the smaller the region supplied by the vessel, the less important its physiological function, and furthermore the more favorable the conditions are for the development of the collateral circulation. This collateral circulation develops almost without interruption during the slow course of arterial inflammation.

But if terminal arteries are affected or if the morbid process involves numerous arteries, then impairment and abolition of the circulation and in connection therewith diminished nutrition and necroses are inevitable.

Death of a fœtus as the result of diseased umbilical and placental vessels, foci of softening in the brain or heart, ulcerations of the skin and mucous membranes are natural results of arteritic processes.

It is not unlikely that syphilitic arteritis also causes occasional fragility of the walls of vessels; the origin of hemorrhagic syphilides may thus be explained. Hemorrhagic forms of syphilis in nurslings are especially frequent. Diseases of vessels in syphilis often occasion hemorrhages in the brain. Bradley has reported a case of profuse metrorrhagia occurring one week after parturition in a woman with syphilis, which he regarded as dependent upon the existing disease. In a man affected with syphilitic ulcerations of the pharynx Bernard had to ligate the common carotid artery on account of a violent hemor-

rhage from the larynx. Undoubtedly many very dangerous hemorrhages which occur during the course of syphilitic ulcerations depend upon perforation of a gumma on the wall of the blood-vessels; but it is not certain in such cases whether or not the gumma originated in the arterial walls, for it is possible that the gummy nodules originated in the parts surrounding the vessel and extended to the latter in the course of growth.

The symptoms of disease of the *veins* also depend upon the extent, localization, and time of development of the disease.

As has been stated above, slight phlebitides in a region which still receives its blood through healthy veins may run their course with extremely slight symptoms.

The Blood.

At the very beginning of the constitutional stage of syphilis some individuals become weak, are easily tired, and are strikingly pale. It is natural to regard these symptoms as due to an anæmia, which has its cause in the morbid condition, even though slight, of numerous lymphatic glands. This condition of *syphilitic anæmia* which was noted by Ricord and Grassi, or as it is also called *syphilitic chlorosis*, improves in most cases, but strumous lymphadenitis may also lead to an increase of the white blood corpuscles, to *leucocytosis* or *lymphatic anæmia.*

If the spleen is affected at the same time, the resemblance to leukæmia becomes still more marked, or a true leukæmia may be developed.

Fr. Mosler has reported a case of extreme leukæmia, which he was able to trace to syphilis. In the course of the constitutional disease there occurred a swelling of nearly all the lymphatic glands of the body and an enlargement of the spleen to four times its natural size, accompanied by an increase in number of the white blood corpuscles. The leucocytosis, which is frequently observed in syphilis, had in this case progressed to actual leukæmia.

From the great importance which has of late years been attached to the bone marrow in the making of blood, we are certainly prepared to find notable changes in this tissue also.

The experiments of M. Litten and F. Orth have in fact demonstrated that, as is commonly the case in grave diseases which lead to cachexia and marasmus, the bone marrow is also subject to a lymphoid transformation in syphilis. Of three cases of syphilis a reddish fatty marrow was found in two cases, a red lymphoid marrow in one. The above-named authors, however, also found much lymphoid

marrow in caries. In the bone marrow of syphilitic persons, nucleated red blood corpuscles, in one case in large quantities, and cells containing blood corpuscles (which occasionally contained nucleated red blood corpuscles) could also be demonstrated.

E. Neumann explains this fact by assuming that in every case of anæmia, though perhaps not without exception, there is an increased functional activity of the bone marrow. In individual cases it may now be possible that this compensatory metaplasia of the marrow passes into a permanent pathological hyperplasia, and may thus, under certain conditions, cause leukæmia. And in truth, preliminary experiments by Litten and Orth have shown that after the induction of artificial anæmia in dogs some of the long bones contain red marrow, and that there is an enormous quantity of nucleated colored blood corpuscles, which are also found in small numbers in the blood.

More minute studies as to the condition of the blood in leukæmia and leucocytosis were first undertaken after the experiments of P. Ehrlich and his pupils. In the year 1879 Ehrlich, basing his classification upon the mode of reaction in the presence of staining agents, distinguished five varieties of leucocytes, each presenting characteristic nuclei. He named these α, β, γ, δ, and ϵ nuclei, and ascribed to the cells with α nuclei, the eosinophile cells, especial importance. According to him an increase of these cells always points to a chronic change in the blood-producing organs. Especially in leukæmia the eosinophile cells are always increased to an exceeding high degree. Later Ehrlich discovered that the presence of cells with neutrophile (ϵ) nuclei is characteristic of myelogenous leukæmia, and that these as well as the eosinophile cells have their origin in the bone marrow. Through the experiments of Hermann Franz Müller and Hermann Rieder this importance of an increase in the eosinophile cells was lessened somewhat, as they were found to be present in non-leukæmic blood up to twenty-one per cent. of the white blood corpuscles. On the other hand, these investigators claim to have discovered morphological differences between the normally present eosinophile cells and those which make their appearance in leukæmic blood.

This difference is denied by Julius Weiss, who also denies the increase of eosinophile cells in different diseases, as he was able to demonstrate their presence only in diseases of the spleen.

Julius Zappert found in healthy men a variable proportion of eosinophile cells up to eleven per cent. of the total number of leucocytes, as had already been stated by Ehrlich. Zappert also maintained that, in leukæmia, we could speak only of an absolute but not of a relative increase of the eosinophile cells, and he corroborated the

findings of Edmund Neusser that frequently a marked increase of eosinophile cells is present in the blood in various skin diseases.

As Neusser found the eosinophile cells greatly increased in the blood in dermatoses, as, for example, in pemphigus, lymphoderma perniciosa, but not in the bone marrow of a patient who died with pemphigus, he concluded that the eosinophile cells may also be formed in the skin. In the same way the kidneys in uræmia and the lungs in asthma were said by him to be the seat of origin of the eosinophile cells.

As regards the number of the white blood corpuscles in general, the experiments made in recent years confirm the view that this is increased in pregnancy, chlorosis, secondary anæmia, in the various inflammatory affections, in malignant tumors, and in the various cachexiæ, as well as in dermatoses.

In view of these facts we must proceed with caution in drawing definite conclusions from the changes found in the blood in syphilis.

In his numerous experiments August Letzius found that the diminution in the amount of hæmoglobin in syphilis was always greater proportionally than that in the number of red blood corpuscles, although the latter were also reduced somewhat; the number of leucocytes, on the other hand, varied within normal limits, as did also the proportion of the uninuclear to the multinuclear forms. According to this the blood changes in syphilitic anæmia are similar to those met with in essential chlorosis, in so far that in both the decrease of the hæmoglobin is greater proportionally than that in the number of red blood corpuscles, and so the individual blood corpuscle contains less hæmoglobin than in its normal condition. The term "syphilitic chlorosis" has therefore been aptly applied to this form of anæmia.

Contrary to this, Stoukovenkoff, Vladislav Bieganski, and Luigi d'Amore have determined that, under the influence of the poison of syphilis, there is a rapid decrease in the proportion of hæmoglobin, as well as in the number of red blood corpuscles, and parallel with this an increase of the white blood elements, among these especially of the lymphocytes; and that these changes occur, as a rule, previous to the appearance of the exanthem. A few days after the beginning of the mercurial treatment the proportion of hæmoglobin and the number of red blood corpuscles increase, and soon attain the normal, while the white blood corpuscles continually decrease in number. The increase of the red blood corpuscles is sooner effected than is the return of the hæmoglobin to its normal proportion. If too much mercury is administered, the proportion of hæmoglobin in the blood again decreases and the red blood corpuscles become fewer.

In hereditary lues also the hæmoglobin is reduced in amount.

In higher grades of anæmia the red blood corpuscles also diminish in number, and we find among them megalocytes and microcytes as well as nucleated erythrocytes. The white blood corpuscles are increased in all their forms, but the myeloplaxes are especially numerous (Johann Loos).

Julius Zappert in his eight cases of lues (macular, papular, and ulcerative forms) was unable to demonstrate an increase in the eosinophile (large) leucocytes; in only one case their number was very slightly increased. It should not be overlooked in all these examinations, however, which were carried on before, during, and after treatment, that preparations of mercury are not without influence on the amount of water in the blood. As is known, Ernst Jendrássik refers the diuretic action of calomel to the inspissation of the blood, and Vladislav Bieganski also mentions that the use of mercury occasions more or less thickening of the blood, independent of any fluids that the patient ingests.

Hermann Schlesinger, who studied the question of temporary and permanent changes in the blood after treatment with mercury, found that subcutaneous injections of the usual solution of corrosive sublimate was always followed by primary inspissation and consecutive thinning of the blood, while the rise of specific gravity was accompanied frequently by a very marked relative increase in the number of erythrocytes, and each fall in specific gravity by a diminution in the number of the red blood corpuscles. In two cases the action of the sublimate was such that a reduction in specific gravity took place directly without a previous inspissation of the blood; but this gave place again to normal conditions after six days at the longest. We are accordingly tempted to look with E. Kaufmann upon corrosive sublimate as a blood poison, which directly destroys the red blood corpuscle. On the other hand, Hermann Schlesinger was unable to detect any blood changes after subcutaneous injections of oleum cinereum during a continued observation of from five to eight weeks. As the syphilitic symptoms nevertheless disappeared, says Schlesinger, it is plain that we are not in a position to draw any conclusions from the inspissation of the blood, that is to say, from changes occurring in it, as regards the absorption of the oleum cinereum.

After inunctions Schlesinger was also unable in eight patients, who were not anæmic at the beginning of treatment, to demonstrate during the whole course of treatment, which lasted many weeks, any or at most only very slight deviations in the specific gravity of the blood; while in two anæmic individuals the specific gravity of the blood during treatment rose slowly but steadily, and parallel with it

there was an increase of the amount of hæmoglobin, but no essential change in the number of the erythrocytes could be demonstrated. Hence Schlesinger is inclined to enlarge Bieganski's propositions to the effect that, in inunction treatment, the density of the blood and the number of the red blood corpuscles are not essentially affected during the entire antisyphilitic course, continued until all syphilitic symptoms have disappeared. In syphilitic anæmia the proportion of hæmoglobin may increase under treatment with mercury, but it does not follow from this that it will increase in the case of a syphilitic patient who is not anæmic.

H. Schlesinger sums up the most important results of his series of investigations as follows: Mercury may, when introduced into the system in large quantities in the form of a soluble preparation, alter the density of the blood for a short time. A preparation suitable for this purpose is corrosive sublimate, after the introduction of which changes in the specific gravity of the blood take place with nearly mathematical accuracy. But the introduction into the body of even large quantities of other preparations of mercury, such as oleum cinereum or unguentum cinereum, may exert no influence whatever on the specific gravity of the blood.

From all this we learn that we must bear in mind many secondary considerations in examining the blood of syphilitics, and especially that, although antisyphilitic remedies favorably influence the condition of the blood, they do so only to a certain degree; and that even the choice of the preparation and its mode of application are not altogether indifferent as regards the effect upon the composition of the blood.

Taking into consideration all the facts above mentioned, it seems to be proved unequivocally that an examination during the course of syphilis will frequently enough reveal distinct symptoms of anæmia.

In individual cases, especially in individuals predisposed to them, syphilis seems to lead to such grave disturbances in the formation of blood as actually to induce *pernicious anæmia*. In this grave form of anæmia the number of the red blood corpuscles is markedly diminished (generally to below one million), so also is the amount of hæmoglobin in the blood.

We should mention also that it is directly characteristic of pernicious anæmia that the diminution of the hæmoglobin does not by any means take place to the same degree as the diminution in the number of the blood corpuscles, but that this coloring matter is found in the individual blood corpuscles in rather increased amount (S. Laache, Kohler). Ehrlich found that unusually large nucleated red blood corpuscles (megaloblasts and gigantoblasts) are found only

in pernicious anæmia; on the other hand, the leucocytes are not increased. Finally fever and capillary hemorrhages belong to the phenomena of pernicious anæmia.

In the *secondary anæmia* complicating cachexiæ of various kinds, the red blood globules are also decreased, but equally so is the hæmoglobin; with this there is an absolute increase in the number of leucocytes, especially the multinuclear forms (Ehrlich).

We must also take into account that pernicious anæmia, although met with in a syphilitic, may be wholly independent of syphilis.

In a case of pernicious anæmia observed by me, the patient was a merchant, 30 years of age, who had become infected six years previously and had been treated with tannate of mercury and iodide of potassium. On account of paralysis of accommodation of the left eye, capillary hyperæmia of the fundus oculi, and infiltrations of the size of a pin's head on the volar surface of the hands, he was again put on mercury, at first with good results. During the second week hemorrhages occurred in the skin and the mucous membrane of the mouth. Mercurial treatment was abandoned, and during the third week hemorrhages occurred in the uropoietic system, so that much blood was voided with the urine. It was only then that I discovered, on questioning the patient, that he had always been in the habit of losing a great deal of blood on the slightest injury (pulling of a tooth, etc.), and that as a child he had suffered from a hemorrhage (after ritual circumcision), which was difficult to control. He was then put on arsenic. In the further course of the disease hemorrhages occurred from the tonsils and the gums, the patient lost flesh more and more, his appetite disappeared altogether, the temperature rose, and he finally died.

Obviously this man had a previous hemorrhagic diathesis, which, reawakened by lues, increased to a pernicious anæmia. I therefore agree with those who regard lues as only an exciting cause, though truly an eminently exciting one. In a few cases (in women) anæmic disturbances had previously existed, as menstruation first made its appearance in three at the ages of nineteen, twenty-one, and twenty-two years, and in others there was present a congenital anomaly which predisposed to anæmia.

Some of the cases of pernicious anæmia complicating syphilis were treated with antisyphilitic remedies. Improvement was noted in a few cases, but how long it lasted is not known; in other cases improvement lasted several months, after which the condition again became very bad. In the greater number of cases antisyphilitic treatment either acted badly or the patient became markedly worse after temporary improvement.

SYPHILITIC AFFECTIONS OF THE GLANDS.

The Lymph Glands.

The indolent buboes which make their appearance a few days after the syphilitic initial manifestation present a paradigma in many respects for the *enlargement of the lymphatic glands*, which is observed later in the course of the disease. Just as the bubo points to an initial affection, present or past, in its periphery, so the enlargements of the lymphatic glands which make their appearance during constitutional syphilis lead us to conclude that irritative syphilitic processes are going on somewhere in the area of their lymph channels, or have gone on there. Lymphadenitides on the neck, the throat, and in the submaxillary region would therefore point to syphilides of the head, the mucous membrane of the mouth or pharynx, in the same manner as enlargements of the cubital and axillary glands are referred to similar processes on the arms. There is no doubt that enlargements of the mediastinal, abdominal, and pelvic glands also have a close connection with irritative processes in the intestinal canal. We observe, on the other hand, however, that later syphilitic products, especially gummata—when not complicated with common suppurative processes—or syphilitic callosities, are only in exceptional cases accompanied by an affection of the neighboring lymphatic glands.

In many cases it is now certain that lymphadenopathies, even outside of the area of primary infection, are observed soon after the generalization of syphilis, occasionally even without the presence of a trace of an eruption in the periphery. This fact may have led Sigmund to the belief that the generalization of the contagium of syphilis at first took place on, and then only through the whole lymphatic glandular system. We have, however, now demonstrated that the contagium of syphilis which has become constitutional probably affects the general integument primarily, but that now and then the skin and the mucous membranes are very little or not at all affected, and in their place the deeper tissues seem to be attacked by preference. When, therefore, enlargement of the glands of the neck occurs without any syphilitic eruption on the head or in the oral cavity, we may search with much greater probability of success for irritative syphilitic processes in the muscles, the periosteum, or even the meninges, rather than assume with Sigmund the direct distribution of the contagium through the whole lymphatic glandular system.

The possible occurrence of syphilitic diseases without a previous affection of the periphery should nevertheless be emphasized. In

such a case the contagium may have entered the glands by the lymph current as well as by the blood current. As regards infection of the glands by way of the lymph current we know, as already mentioned, the remarkable fact that this is mainly encountered during the early stage of syphilis. The morbid changes of the lymphatic glands in the neighborhood of the initial lesion have already been minutely considered. The irritative processes occurring after the generalization of the syphilitic contagium produce in the neighboring lymphatic glands, probably not as regularly as the initial lesion, but still frequently enough, changes similar to those occurring with the latter. Macules, still more papules and pustules, according to their localization, are followed by enlargement of the glands of the neck, throat, and elbows, the axillary and subclavian glands, and also the glands of the thigh and of the inguinal region, if they have been previously spared on account of the extragenital seat of the initial lesion. It is, however, also probable that irritative conditions in deeper-lying tissue may also be the cause of such adenitides. At the same time we occasionally observe that in a series of lymphatic glands, situated in the course of the lymph current, the peripheral glands are more affected at one time, at another the central glands. It is therefore also quite possible that the indolent buboes of the groin may remain absent in the case of an initial lesion of the genitals, and in their stead the glands of the pelvis become enlarged.

We have above expressed the belief that the contagium of syphilis in all probability retains its virulence, that is to say, its power of infection, only so long as it is able to produce irritative processes in the patient. In this stage the contagium seems also to possess an increased power of enlarging the neighboring lymphatic glands.

Pathological Anatomy.

The lymphatic glands present in the beginning an irritative swelling and hyperæmia, an increased flow of serum, and an enlargement of their cells; the enlarged follicles of the gland appear as grayish-white dots. In its further course the hyperæmia diminishes and new connective tissue is developed in the stroma from which an even, whitish, grayish-white, reddish-white, or gray appearance results (Virchow). The course of the process within the glands, which is as a rule slow, leads to an imperfect fatty metamorphosis with inspissation, for which Virchow has coined the expression, *caseous metamorphosis*. The anatomical picture developing in this process is described by him as follows: The inguinal glands are some the size of a plum and whitish externally, others of a bright reddish color,

presenting on section numerous caseous foci the size of a cherry pit or smaller; some of the latter are white and dry, others of a pasty consistence. While, therefore, the cellular hyperplasia attracts attention in the early period, the later affections are characterized by induration, cirrhosis, and cheesy degeneration (Cornil). The capsule of the gland appears little or but passively changed in the course of syphilis, and it is only in the strumous buboes of lues that the connective-tissue framework presents a high degree of thickening and sclerosis (Cornil).

In the course of the irritative stage of syphilis the lymphatic glands grow to tumors the size of an almond or a hazelnut, at times even larger, which are freely movable, quite firm to the touch, and but slightly tender. Those glands which are situated between tense skin and bone, as those on the processus mastoideus, are, however, less movable and are painful on pressure.

As in the initial stage, we also here occasionally find a gland standing out prominently above the others in size; but very often, after generalization of the contagium, we find nearly all of the glands of the affected group participating equally in the enlargement.

In many cases the enlarged glands diminish quite rapidly, and occasionally disappear with the subsidence of the irritative symptoms; frequently, however, they persist almost without change for months after the latter have disappeared. Accordingly, enlargements of the lymphatic glands not very rarely present the only or at least the most evident sign of a past syphilitic infection.

The older the syphilis is, the less frequently do otherwise healthy individuals suffer from recent complicating affections of the neighboring glands and relapses; and gummatous products also, in such cases, do not seem as a general rule to cause enlargement of the lymphatic glands. "If you find diseased ganglia with late symptoms," Ricord says, "by searching you will find other causes for their occurrence; the impression which they give will be different, or the patient will tell you that these enlargements had persisted after the earlier symptoms had disappeared."

The variety of affections of the lymphatic glands, discussed so far, which we might designate as diffuse, is subject, in cachectic individuals or such as suffer from scrofula or tuberculosis, to similar deviations from the typical course as the buboes which accompany the initial lesion (which see). The glands enlarge into strumous tumors the size of a walnut and larger still, which coalesce and form quite a considerable cluster; their mobility is early abolished by adhesions which the capsule of the gland forms with the surrounding connective tissue and the skin; purulent disorganization and soft-

ening then take place in the periadenitic tissue and in the gland itself. The skin becomes perforated at one or more places, the glands are bathed in pus, and fistulous passages are formed ramifying in every direction. The complete destruction of the gland by suppuration in cases left to themselves takes place in an exceedingly slow manner.

In debilitated individuals or those who suffer from other dyscrasias, similar changes are observed in the lymphatic glands in connection with gummata; or inflammation of the lymphatic glands, which sometimes terminates in suppuration, occasionally results from neglected gummatous ulcerations.

Gummatous affections of the lymphatic glands are met with here and there. Extensive gummatous changes have been found in the superficial maxillary glands of the neck, the tracheal and bronchial glands, in the lymphatic glands of the œsophagus, of the lesser curvature of the stomach, and of the mesentery, and in the portal and lumbar glands. In the accessible lymphatic glands we find the infiltration as a rule extending also to the surrounding tissues and the skin.

A gumma of the gland may in its progressive course form a distinct tumor, which is intimately connected with the parts about and the skin, and in which vessels and nerves are firmly embedded; the tumor is firm, with here and there an occasional spot of softening, and of variable sensitiveness. Softening, however, is usually progressive, the skin also then becomes involved in the destructive process, and an ulcer forms the base of which is connected with softened or caseous parts of the gland. Occasionally the bursting of glandular gumma leads to ulceration of the skin, which then not infrequently assumes a serpiginous character and extends over a large surface. I have repeatedly seen such gummatous lymphadenopathies (*gummatous lymphoma*) in the groin, the thigh, the throat, and the preauricular and orbital regions. In the cases observed by me the glandular gumma of the inguinal region existed alone, and had followed a scleradenitis; but in other cases the gummatous lymphadenitis of the preauricular region, the elbow, or the throat had been added to gummata of the muscles and of other localities, after syphilis had existed for some years. Similar observations have also been reported by Rollet, Campana, S. Lustgarten, Walter Guttmann, and others. The gummatous adenitis is characterized by a very slow course, although a general antisyphilitic treatment conjoined with energetic local measures may effect a more rapid cure than in those cases of syphilitic adenitis occurring in scrofulous individuals which go on to suppuration. The cicatrix remaining after recovery is adherent to the deeper tissues. Occasionally remnants of the glands may be distinctly seen in the deeper parts or in the immediate neighborhood.

Diagnosis.

We will mention here only a few of the non-syphilitic affections which are also accompanied by adenopathies. Eczema, lupus and other tuberculous skin affections, still more frequently carcinoma and prurigo, are among the causes of enlargement of the lymphatic glands; but, if we carefully consider the affection localized in the area of the lymph current, the nature of the pathological process going on in the glands will hardly escape our proper judgment. The differences which exist between *carcinoma* and *lupus* on the one hand and syphilis on the other have already been discussed. *Prurigo* usually changes the skin on the extensor surfaces of the upper and lower extremities, especially of the leg and forearm, in the most marked manner, and besides is characterized by intense itching, which latter may also be said to occur in a greater or less measure in *eczema*. When the peripheral disease has healed, quite characteristic changes (cicatrices, pigmentations) are usually left behind, by which the original affection may be recognized. In milder cases, however, these symptoms may be absent, and we are then deprived of their aid in diagnosing the affection of the glands.

Diffuse syphilitic adenitis in otherwise healthy individuals may be easily recognized by the fact that the glands present only as small tumors, the size of an almond or a hazelnut, rarely larger, which are not painful, are readily movable and firm; they remain in this condition for some time, and only rarely go on to suppuration. Besides this several glands of the same region always participate in the affection. Quite frequently the same condition is repeated in different groups of lymphatic glands. *Scrofulous* and *tuberculous* lymphatic glands form very large tumors and very early become firmly fixed. Softening and partial suppurative destruction are rarely absent. Bursting of the abscess through the thinned and undermined skin is the usual course. We are not always able to demonstrate the presence of tubercle bacilli in the pus.

It may, however, also happen that a scrofulous or tuberculous individual becomes syphilitic or that a syphilitic person becomes scrofulous or tuberculous, and in the diagnosis of such a case all side factors must be carefully taken into consideration. As a rule in these cases the scrofulous or tuberculous process prevails over the syphilitic. Gummatous lymphomata, which are met with in connection with other evident signs of syphilis, are easily recognized. If a lymphatic gumma occurs singly, however, we must guard against mistaking it for a scrofulous (tuberculous) lymphoma, or for actino-

mycosis or a malignant neoplasm. As regards this, the reader is referred to what has been previously said, but we may mention that the difficulty experienced in the differential diagnosis is nevertheless sometimes great. As a matter of fact, such formations have occasionally been mistaken for malignant tumors and have been extirpated (B. v. Langenbeck, Friedrich v. Esmarch); only the cure of the subsequent relapses by iodide of potassium made the diagnosis clear. We should therefore never neglect to institute antisyphilitic treatment in doubtful cases.

As to the *importance* of the adenopathies, in the further course of the syphilitic process, our knowledge is as yet not so definite as we might wish. In all probability the contagium of syphilis reaches the lymphatic glands at a very early period. It may be that a part of it is here destroyed, a part, however, only finds a temporary resting-place, from which it again enters the circulation, after a certain time, to lead to recurrences by way of metastasis in some other portion of the body (see above).

In some cases also mechanical effects, which result from an enlargement of the lymphatic glands, make their appearance. Thus occur obstructions in the lymph channels or veins, or neuralgias from pressure on the different nerve plexuses.

What has been said regarding the affections of the lymphatic glands in the course of syphilis may also be applied in great part to the faucial, lingual, and pharyngeal *tonsils*, all of which in structure and function resemble each other, except that in these parts ulceration is more frequently observed.

The Lymph Vessels.

Evident as it is that the contagium of syphilis must pass through the *lymphatic vessels* on its way to the lymphatic glands, we have as yet but little information as to syphilitic affections of the lymph channels. According to the clinical symptoms, lymphangitides, which on account of their form I have called scleroses of the lymphatic cords (*Lymphstrangsclerosen*), are of frequent occurrence between the initial lesion and the buboes belonging to it. Much less frequently do we meet with affections of the lymphatic vessels in the later stages of syphilis.

Clinically, I have been able in several cases of constitutional syphilis, especially during the irritative period, to diagnose firm, nodular, only slightly tender cords as diseased lymphatic vessels, because they could be traced to a firm, enlarged lymphatic gland. I have seen these on the throat, the neck, the abdomen, and the thigh.

These lymphangitides persist a very long time, and their involution may take several months for its accomplishment. I have never seen them break down and go on to destruction.

Gummata of the lymphatic vessels are very rarely observed, but I have found them quite marked on the upper and lower extremities. The gummatous nodules, in places softened and broken down, are arranged at the side of the lymphatic vessels, joined to each other and to the lymphatic gland by firm cords.

The Spleen.

Affections of the spleen during the course of syphilis are of very frequent occurrence. Aside from the *enlarged spleen* caused by amyloid degeneration, that caused by hyperplastic changes has been frequently demonstrated. Virchow distinguishes two forms here, a flaccid or soft and an indurated form; the latter occasionally resembles the amyloid form.

Distinct *gummata* of the spleen are more rare. The results obtained by A. Haslund from the post-mortem material of the Copenhagen Commune Hospital were very interesting in this direction. Among forty-four adults who had died of acquired syphilis, twenty-seven presented hyperplasia and three amyloid degeneration of the spleen. Gummatous affections of the spleen were not found.

Disease of the spleen in the course of syphilis may sometimes be found very early. Methodical examinations of the spleen undertaken in my clinic gave the following results: In thirty cases of recent syphilis the spleen was found enlarged eight times; in four of these cases there was a previous history of malaria. In one case, however, we found a diminution in the size of the spleen at the same time that the other syphilitic symptoms diminished in intensity. In three cases the spleen became enlarged under our own observation. Similar results were obtained in my clinic from observations carried on in patients, of whom some were suffering from the initial lesion, while others were in the early stages of constitutional syphilis. In one case it was possible to observe the gradual increase in the size of the spleen. In three cases the diminution of the tumor under antisyphilitic treatment was very evident.

In advanced syphilis the involvement of the spleen may be frequently enough seen; it very commonly accompanies syphilis of the liver. Ducrey was able in one case to demonstrate by microscopical examination that an atrophy of the liver and spleen, existing together with a luetic stenosis of the pharynx, could be referred to an endarteritis syphilitica.

The Thymus and Thyroid Glands, Suprarenal Capsules, and Pineal Body.

In closing this section the syphilitic affections of some organs whose physiological functions to a great extent are not yet fully determined may be briefly mentioned.

Since the time of Matth. Tiling (1634–85) morbid changes of the *thymus* have been discovered in the bodies of syphilitic persons here and there.

In the *thyroid gland* I once saw in the case of a man, forty years of age, several dense, distinctly circumscribed infiltrations the size of a chestnut and quite tender. The patient was poorly nourished and had other signs of lues.

Gummata of the thyroid gland have been met, together with gummata of other organs, especially in the new-born.

Gummata (Birch-Hirschfeld) or gumma-like degenerations (C. A. Gordon) have also been seen in the *suprarenal capsules* of patients who had died with symptoms of Addison's disease.

Gummatous deposits are also recorded as present in the *pineal body* (Carl Weigert, Barbacci, F. v. Birch-Hirschfeld).

SYPHILITIC AFFECTIONS OF THE GENITO-URINARY ORGANS.

The Kidneys.

The kidney may be affected in several ways in the course of syphilis. We find acute, subacute, or chronic Bright's disease, granular kidney, gummatous infiltration, and amyloid degeneration, each and all of these forms occurring singly or variously combined. In the cases operated on by James Israel, an extensive peri- and paranephritis was present together with an interstitial and gummatous nephritis.

The statistics of the various affections of the kidneys in syphilitics may be obtained from a tabulation by Spiess, who collected 220 cases from the post-mortem records of the Charité. In 147 cases affections of the kidneys were present; among these were 42 cases of amyloid kidney and 7 cases of gummatous kidney. Congenital syphilis was represented by 34 cases, of which 10 showed kidney disease, 3 cases presenting amyloid degeneration. Gummata are not mentioned as occurring in a single case of hereditary lues. E. Wagner based his observations on the post-mortem records of 63 cases. Gummata were

found in 3 cases, amyloid degeneration in 35 cases; the other cases were divided into 8 of acute, 4 of chronic Bright's disease, 7 of granular kidney, and 6 of unilateral atrophy of the kidney.

H. v. Bamberger, who attempted to determine the relations of Bright's disease to other diseases from a study of 1,623 post-mortem examinations, found in 49 cases that syphilis was the cause. Gummatous infiltration does not seem to have been taken into consideration in these statistics. Changes characteristic of lues are found only in the gumma, and occasionally the latter attains a large size in the kidney. Nephritis (Bright's disease) and many of its sequelæ (contracted kidney), which very often occur in cases with syphilitic symptoms, do not in themselves offer anything peculiar to syphilis. It is therefore quite difficult to decide in a specified case whether the disease accompanies lues only accidentally or stands in a direct relation with the infection. The amyloid kidney following syphilitic processes is not often characterized by any special sign. The very same degeneration is found equally in tuberculosis, bone affections of long duration, and other disturbances leading to cachexia.

Sigmund Rosenstein, however, emphasizes the occurrence of amyloid degeneration in syphilis even without cachexia, and the occurrence with especial frequency of the combination of amyloid kidney with contracted kidney, which, as many observers believe, is peculiar to syphilis. The contracted kidney of this form is usually dense and heavy, and the individual granulations on the surface are uneven compared with the ordinary contracted kidney. Hypertrophy of the heart is also absent in the syphilitic contracted kidney.

Symptoms.

The clinical symptoms of syphilis of the kidney do not as a rule present anything peculiar. We must here rely mainly on the discovery of signs of a past or still present syphilis in other organs, and also on the previous history—if it is reliable.

It was formerly believed that the kidney became diseased as a rule only several years after infection; this is not the case, however. H. N. Descost, Perroud, and Lancereaux have noted that the kidney becomes affected at a very early stage of syphilis, and E. Wagner describes a Bright's disease occurring six weeks after infection, which disappeared at the same time with the other symptoms of syphilis, following the institution of specific treatment.

Aside from the fact that albuminuria, even cylindruria in a slight degree, may occur transitorily, I have repeatedly demonstrated, since I have given more thought to the condition, that these symptoms of

kidney affections may exist at the beginning of the constitutional disease and may continue for a long period. Affections of the kidneys of this variety are either due, when other etiological factors can be excluded, to the direct action of the contagium of syphilis on the substance of the kidney, or the affection is based on the excretion of the products of metabolism eliminated by the contagium vivum of syphilis. In the first case the nephritis would be an *infectious* one, in the latter a purely *toxic* one, namely, a *syphilotoxic* infection. Kidney affections of this kind demand a direct antisyphilitic, frequently also a mercurial treatment. I have, however, also met with cases in the later period of syphilis (in general much more rarely) in which the amount of albumin in the urine was markedly diminished during and after a course of antisyphilitic treatment.

Diagnosis.

As regards the diagnosis it may be stated that it is certainly not easy in an affection of the kidney, even when this occurs in a manifestly syphilitic subject, to determine that lues is positively the cause; but just as little can this be excluded. In general in a case in which a person, previously healthy and without any symptoms referable to the kidneys, acquires syphilis, and in which in the course of the development of the constitutional disease every other cause being excluded, signs of nephritis make their appearance, we shall be fairly justified in regarding the renal trouble as a part of the general affection. The case is different if nephritis is found early or late during the course of syphilis. Here we must remember the possibility that the kidney affection may be independent of the lues, having perhaps already existed previous to the infection of syphilis. Deviations in the amount of albumin in the urine, which periodically contains blood cylinders, blood, and cellular detritus, may point to a gumma of the kidney. In amyloid kidney, albuminuria is nearly always present. In this case the degeneration, no matter whether due to syphilis or to some other disease, is frequently enough found in other organs, and at times is especially marked in the spleen and liver.

We should not forget, however, that an affection of the kidney occurring in a syphilitic subject may also be produced by mercury, being then a toxic affection; it is certainly more frequently developed in the course of an antiluetic mercurial treatment than is generally supposed. To Fürbringer belongs the credit of having demonstrated by close observation that the common mercurial treatment may in fact cause an excretion of albumin. My own observation, when my attention was drawn to this subject, convinced me that albuminuria

not very rarely makes its appearance even during a mild course of mercury, and that therefore the presence of albumin in the urine is as important a symptom of intoxication as are the mouth and intestinal affections. I plainly expressed my views on this subject at the Tenth International Medical Congress in Berlin. In this connection the observations of Edward Welander, who demonstrated that in the course of a mercurial treatment not only albuminuria but occasionally also the excretion of no small number of tube casts takes place, are quite instructive. It is easily shown that albuminuria or cylindruria or both will be more frequently met with during energetic treatment by mercury. It is, however, remarkable that these nephritic symptoms, usually make their appearance even during the couse of a mild internal treatment with mercury.* Should we, therefore, observe the occurrence of albuminuria or cylindruria in a patient who is under mercurial treatment, or is still under the effect of a previous mercurial course, the possibility of a toxic nephritis is to be considered. The possibility will become a probability if these symptoms have developed only during the course of the mercurial treatment. In cases of this kind the presence of mercury in the urine can also be demonstrated. When the mercury is stopped, the symptoms of nephritis subside and finally disappear totally and permanently. Large (toxic) doses of mercury will directly produce calcification of the convoluted tubules of the kidney (J. L. Prevost, Saikowsky).

Gummatous nephritis, according to its various stages, will cause the abnormal ingredients of the urine to make their appearance in a very variable manner. If the affection is unilateral, the excretion from the diseased kidney may cease altogether when the pelvis of the kidney becomes obstructed by the growing gumma, while the healthy kidney secretes normal urine. Errors may, however, also occur here. Thus I once made a diagnosis of gummatous nephritis in a patient who had recent gummata elsewhere, together with numerous rests of earlier syphilitic lesions, from the variable amount of albumin and tube casts present in the urine, and from the existence of a localized tenderness in the kidney; but in the further course of the disease the voiding of echinococcus cysts in the urine revealed the true condition of affairs.

* As we know, cylindrical casts are occasionally found even when the kidney is normal. When, therefore, we speak here of cylindruria a pathological excretion tube of casts is always to be understood.

Prognosis.

The affection of the kidney described as occurring in the beginning of syphilis runs a favorable course as a rule; otherwise the issue is very often unfavorable. Even in grave cases, however, when a correct diagnosis has been made early, a favorable change may be expected from antisyphilitic treatment, even when we are dealing with amyloid degeneration, which must of course not have progressed too far. Every clinician has undoubtedly met with cases of albuminuria which have also improved or disappeared wholly together with the other syphilitic symptoms in the course of treatment. Gummata permit of a comparatively favorable prognosis for the reason that frequently a portion of the parenchyma of the kidney, which has retained its function, persists by their side. The prognosis is still more favorable when the gummatous infiltration or the disease itself is unilateral. Should a greater portion of the kidney or even the whole organ become atrophic, the loss of its functions may still be compensated by an hypertrophy of the other kidney, in case this has not taken on amyloid degeneration in the mean time. We may note here, in parenthesis, that quantitative and qualitative changes in the urine may also be occasioned by causes external to the kidneys; I refer principally here to diabetes mellitus and insipidus. Although the etiology of *diabetes* is still very obscure, we know at least that the affection may be referred in part to disease of the nervous system, in part to that of the digestive tract (pancreas and liver). It now appears that in the course of the syphilitic process the organs referred to may also become diseased in such a manner that diabetes is produced. According to Fr. Th. v. Frerichs syphilis stands at the head of those, among the constitutional diseases, which may be followed by diabetes, when luetic changes occur in the brain and its meninges or in the medulla oblongata. Diabetes insipidus, however, may also, as we learn from certain isolated experiences, be associated with syphilis.

Observations of definite facts are sufficiently convincing to me and to others that a syphilitic diabetes exists. Several clinicians, however, among these Cantani, take the view that there is in these cases only an accidental coincidence of syphilis and diabetes. At all events I cannot fail to point out that we must be very careful in the explanation of observations bearing on this, as glycosuria and polyuria may also be produced by many other causes, as has been shown by v. Frerichs in his monograph on diabetes. We must not forget particularly that the action of mercury in the organism is very fre-

quently to produce an increased appetite and, dependent on this, increased thirst; with this an increased excretion of urine goes hand in hand. These symptoms have frequently been noticed by me and other clinicians. Under certain conditions we know that preparations of mercury are employed as diuretics. In judging of these cases we shall therefore have to exclude other causes, and determine especially whether the patient is not under the influence of mercurials. Furthermore, we should remember that mercurialization may cause mellituria. Saikowsky in his experiments found more or less sugar present in eight rabbits out of twelve which had received chloride of mercury; here of course we refer to large doses of mercury, following which v. Mering also found sugar in the urine, and to a mellituria which is purely temporary. It is, however, possible that mercury in therapeutic doses might also have a similar effect. Chevallier, indeed, mentions having observed diabetes mellitus following a mercurial treatment; I myself have observed this as little as others (Kussmaul, Lewin).

We must also mention *hæmoglobinuria;* this has occasionally been observed in syphilitics. It is possible that the metabolic products of the contagium of syphilis, like many other poisons, produce an increased destruction of the erythrocytes with resulting hæmoglobinuria. In what manner periodical (paroxysmal) hæmoglobinuria is produced is still more obscure. It is therefore not an easy matter to say whether the results obtained in this affection with antisyphilitic treatment would warrant our assuming a connection between the two diseases. According to some observers (Ponfick) periodical hæmoglobinuria has occurred immediately after a mercurial treatment. Morbid changes have been noted also in other portions of the urinary apparatus in conjunction with syphilitic symptoms elsewhere. But in general few cases of this kind are to be found in any but the most recent literature.

The Urethra.

With the exception of the syphilitic initial lesion in the urethra (see above), *early manifestations* are only very rarely seen in this portion of the urinary tract. I have seen them occasionally. Thus I once found, in examining the urethra with the endoscope, the mucous membrane infiltrated in places in a circular form, or only on one or the other side, swollen, red, and secreting more mucus than the other parts; at another time there were circumscribed swellings and redness, together with a stubborn, small-sized, papular syphilide. Occasionally these small papules will lead to circumscribed erosions. As a rule no marked secretion is present with these affections of the

urethral mucous membrane; it is only when the papular infiltration is extensive that we find an increased secretion. This occurred in a woman, twenty-one years of age, who was treated at my clinic for a papular syphilide and a stubborn, exceedingly painful urethritis. After repeated examinations of the urethral secretion for gonococci had resulted negatively, and the condition did not improve in spite of the use of otherwise well-acting injections, an endoscopic examination was made (which is a routine practice with me in chronic cases). This revealed swelling of the posterior plane of the urethral mucous membrane throughout nearly its entire length, and also a few distinct plaques. An injection into the urethra of a twenty-per-cent. oleum cinereum was ordered, and it put an end to the troublesome condition in a few weeks. Occasionally it is difficult to distinguish herpes-like erosions from true herpes of the urethra.

Later forms of syphilis have been observed somewhat more frequently in these parts, but they are on the whole quite rare. Syphilitic ulcerations of the bladder have been carefully described by Proksch. One of the least doubtful cases was one reported by Virchow. The patient was a woman, eighty-four years of age, who had callous cicatricial tissue in the urethra and bladder, besides other symptoms of syphilis. Tarnowsky has reported the case of a four-year-old child who had been infected by its nurse per os; moist papules and ecthyma pustules covered the whole body, the mucous membrane of the oropharyngeal cavity was marked with ulcerated papules and fissures. In the further course of the disease the child, who had an unhealthy appearance, felt pain on urinating and when pressure was made on the urethra, which was hard to the touch. At the post-mortem examination superficial syphilitic ulcerations were found in the bladder, the liver was syphilitic, and the lung was hepatized.

Gummatous affections of the urethra have been observed by me several times. Of these I may mention a gumma larger in size than a hazelnut, situated in the fossa navicularis, which formed by its destruction an ulcerating cavity in which residual urine was undergoing putrid decomposition. In the absence of positive data a malignant neoplasm was suspected, the patient being an old man over sixty years of age. The administration of iodide of potassium brought about a perfect cure. In another old man, sixty years of age, I found superficial serpiginous ulcerations with cicatrization in the prostatic portion extending to the bulbous portion of the urethra; from this an infiltration the thickness of the thumb ran to the anterior surface of the scrotum. Iodoform applied locally and iodide of potassium internally brought about a marked improvement.

Syphilitic ulcerations of the mucous membrane of the urethra are easily discovered by means of the endoscope. Gummata of the urethra from the size of a pea to that of a nut (the latter would obstruct the lumen of the canal) are very rarely encountered. Ulcerations of the urethra caused by gummata, which have their seat in the corpora cavernosa, are more frequently observed. In one of my cases a gummatous infiltration of the corpus spongiosum, which had nearly transformed the entire pendulous portion into a nodular mass the size of a finger, led to a perforation externally and into the urethra, that is to say, to a fistula. About the opening the infiltration caused contraction, behind which the diseased urethra bulged out when urine was voided. From the meatus as well as from the opening of the fistula a thick granular pus could be expressed. The urine was made turbid in every specimen by masses of a similar appearance. During an erection the penis was curved in a downward direction. The endoscopic examination, which became possible after a gradual dilatation of the anterior portion of the urethra, showed the mucous membrane of the urethra in the neighborhood of the diseased portion the seat in part of cicatricial strictures, in part of circumscribed areas of infiltration projecting into the lumen of the urethra, which distorted the canal in many ways. The mouth of the fistula could easily be recognized through the endoscope after a sound had been introduced into the external opening. After specific treatment had been instituted the retrogression of the infiltration could be followed most clearly by means of my illuminating endoscope.

I have repeatedly observed gummata situated on the urethral caruncle in women.

Besides the changes which may be demonstrated either by the touch or by illumination, there is also present a more or less copious discharge from the urethra. The discharge is either purely purulent or serous, whey-like, sometimes mixed with particles of tissue, or it may even be ichorous and foul-smelling. Pain may or may not be present. Occasionally the symptoms of stricture are present.

The Penis.

It goes without saying that the external genitals are of especial importance in the first infection with syphilis; but the disease after having become constitutional often deposits its early products with especial predilection on these parts. When discussing the initial lesion, syphilitic roseola, and the papular syphilide, we entered more minutely into these conditions.

More infrequently do we find *gummatous* products here. They

consist of infiltrations of the size of a lentil to that of a bean or larger, in the glans penis or in the corpora cavernosa, which are as a rule painless, and are discovered by the physician or patient only as the organ may be casually touched, when they are felt as firm nodules. In my experience, which corresponds to that of others (Fournier, Edward Welander), the gumma occupies by preference the site of the initial lesion. I have several times observed a very early transformation of the remains of a chancre on the genitals (glans, etc.) into serpiginous gummatous ulcerations. The gummata of the glans and the prepuce break down early, as a rule, on account of their superficial position, and give place to large, sharply defined ulcers of various sizes, frequently in the region of a follicle becoming very deep, and occasionally presenting a serpiginous character.

In the corpora cavernosa we frequently observe the absorption of gummata and their transformation into callosities; but softening and ulceration may also occur here and give rise to large and deep ulcerating cavities, which may perforate into the urethra. If large portions of the corpora cavernosa have been invaded by the gumma or the callosity, there will occur after healing, even under usual conditions but more markedly during erection, a flexure or curvature of the penis (chordee) in the direction of the diseased side. Ricord mentions a case of this kind in which the penis formed a perfect circle. In an old man, who was under my care for gummatous ulceration and destruction of nearly the entire glans and of both corpora cavernosa, the penis healed in the shape of a small hook-like mass.

Diagnosis.

It is by reason of the localization that an initial lesion rather than a gumma is usually suspected when an infiltration is present on the genitals, the more so as ulceration very frequently occurs in either case.

The reader is therefore referred to the description of these lesions given in previous sections of this article, and he is especially reminded that the neighboring lymphatic glands hardly ever remain unchanged in the case of an initial lesion. The diagnosis becomes much more difficult when the gumma has developed on the site of a previous initial lesion, or has even directly arisen from an initial lesion, for the reason that distinct remains of the bubo are as a rule still present.

Small, superficially seated gummatous nodules of the penis might readily be mistaken for *papules*, like those of any other portion of the skin. The possibility of this mistake is also present when the gummata are ulcerated, since papules, especially in this region, are also

liable to erosions and ulceration. We must therefore remember what has been previously said concerning the distinguishing characteristics of the two lesions.

Inasmuch as, in the case of a *syphilitic pustule*, ulceration follows the pustule, and frequently lasts much longer than it, it will certainly not always be easy to decide whether a syphilitic ulcer on the genitals has followed a pustule or a gumma. Here we must decide according to the different mode of development of the two syphilitic products. Furthermore, syphilitic pustules only very rarely make their appearance on the genitals alone, and we therefore find pustules present at the same time in some other part of the body.

There is danger of mistaking broken-down gummatous nodules of the glans, as well as of the genital organs in general, for *venereal ulcers* (chancroids).

Gumma of the penis may, however, also be mistaken for *carcinoma*, and *vice versa*. To avoid unnecessary repetition the reader is referred to the general explanation given previously, and we will here only repeat briefly that gummata rarely cause enlargement of the lymphatic glands, while involvement of the glands is a general rule in carcinoma.

Gummatous cavernitis (inflammation of the corpora cavernosa) can hardly be mistaken for that due to a gonorrhœa.

It should be remembered that callous nodules, ridges, or plates occasionally exist in a corpus cavernosum, which cannot be referred to syphilis as a cause. I have more than once found such a condition, but was unable to learn anything of its etiology. In a few of the cases I was inclined to assume a deposit of urates.

The Testicles.

The testicle is much more frequently found diseased in the later stages of syphilis than the penis.

Pathological Anatomy.

Anatomically our knowledge of syphilis of the testicles (sarcocele syphilitica) dates from Virchow, who described graphically its analogy to syphilis of the liver. We distinguish a simple syphilitic orchitis and a gummatous form.

In *orchitis simplex* a chronic indurating new growth arises from the albuginea, more frequently from the septa and from the connective tissue which runs along the seminal ducts, which involves larger or smaller portions of the testicles, producing at first enlargement, later contraction of the gland. The surface is smooth when the process is equally diffused. As a rule, however, the morbid process is

confined to circumscribed parts, which then stand out as hard nodules, which are converted into as many depressions after contraction has taken place. According as the testicle itself or the albuginea is the principal seat of the disease, we speak of an *orchitis* or *periorchitis syphilitica* (Ricord's *albuginitis syphilitica*). Small exudations into and thickening of the tunica vaginalis are rarely absent.

The gummatous process is as a rule combined with simple orchitis in such a way that smaller or larger gummatous nodules seem to be deposited in the connective-tissue growth; these at times go on to absorption, at times become calcified or cheesy.

According to the researches of L. Malassez and P. Reclus smaller nodules are always first developed and then cause a sclerosis and atrophy in the neighborhood—Virchow's *orchitis syphilitica simplex.* The *orchitis gummosa* of Virchow these authors refer to a necrosis not alone of gummatous foci but also of the sclerosed parts.

The affections mentioned usually develop in the testicle or at least originate here. The epididymis, although more rarely affected independently, is still occasionally primarily attacked.

Symptoms.

Clinically we find that the testicle may become affected early, but frequently it is only after syphilis has existed for some time, even many years after infection, that the gland is attacked. When it is affected during an early period of syphilis we find an uneven and painless swelling of the epididymis, which, even within a few months after infection, is bilateral. It frequently escapes the patient's notice entirely on account of its painlessness. In one of my cases there was an only slightly tender infiltration, about the size of a chestnut, at first on the head of one and soon after on the head of the other epididymis, which was noticed four months after the appearance of the initial lesion, and which improved in a few weeks under the application of emplastrum hydrargyri. Occasionally the affection does not confine itself to the epididymis, nor is it painless in its course, as is illustrated by the following case:

The patient was a carpenter, 30 years of age, who had never previously suffered from any disease of the genitals. He was treated with inunctions at my clinic on account of a recent chancre and a subsequent macular syphilide, and was dismissed cured. A few days later, about sixteen weeks after infection had taken place and fourteen weeks after the appearance of the initial lesion, he was compelled to return to the hospital on account of pain in both testicles. A swelling was found on the external surface of the upper part of the left testicle, the size of a hazelnut, smooth and prominent, which was

very painful when touched, and in addition there was a diffuse swelling evenly distributed over the testicle, together with epididymitis of a less degree. The skin already contained gummatous nodules from the size of a pea to that of a bean at various points. The patient was greatly depressed in spirits, and also complained of vertigo.

The syphilitic affections of the testicles are, however, not so painful, as a rule, as in the case just described, nor do they make their appearance so early. They are generally developed, as has been said, after syphilis has existed for some time. The enlargement of the testicle takes place very slowly, and is accompanied by a very slight pain or a feeling of dulness and weight in the scrotum. The increase in size is not uniform, but the surface of the gland presents hard prominences here and there, or the entire surface is uneven. Occasionally also there is a moderate effusion into the cavity of the tunica vaginalis propria. The affection usually arises from the testicle itself or from its covering, but when the infiltration increases or when it has its seat in the vicinity of the epididymis, the latter is usually also involved. Gumma of the testicle rarely suppurates, but in the great majority of cases the morbid product is in part absorbed and in part becomes contracted. Destruction of the secreting portion of the gland is rarely avoided, and with it and in proportion to its extent occurs a diminution in the amount of semen secreted or even total aspermia, or a decrease of sexual desire and impotence.

At the end of many months, the testicle is found diminished in size; its general shape may be preserved, the surface remaining smooth, or else we find depressions alternating with elevations. At times the organ is reduced to a shapeless nodular rudiment of a testicle. The epididymis being affected more rarely and to a lesser degree as a rule, we find this part usually of normal configuration with only here and there indurated and thickened portions or cicatricial contractions.

This disease of the testicle does not affect the general condition of the patient to any appreciable extent, especially when it runs its course without pain. Sometimes there is a depression of spirits induced by the knowledge that the disease has attacked an organ of generation. I have, however, met with cases in which there was great pain radiating towards the leg of the same side, so that walking and standing were at times made difficult. Occasionally the gummatous infiltration forms a tumor of considerable size, and foci of softening are found in it; when this occurs all the coverings of the testicle are generally also involved. Should these become perforated, which is, however, only rarely the case, the gumma will grow exuberantly fungus-like towards the surface, as a soft, in parts necrotic

granular mass—*fungus testiculi syphiliticus*. The fungus is usually accompanied in its first development by pain, which decreases in the further course of the disease and frequently disappears altogether. We find a fleshy tumor from the size of a chestnut to that of an egg or a man's fist, which exudes necrotic particles and much pus; it is narrowed somewhat towards its base, and is connected with the substance of the (diseased) testicle. The skin is as a rule reddened or somewhat cyanotic, infiltrated, and adherent to the testicle together with the other coverings of the gland; in rare cases it surrounds the neck of the fungus in the form of a thin, sharply cut border, and is then movable to a slight extent.

After having existed for some time, the fungus becomes smaller, partly by absorption, but more by a partial necrosis with extrusion of the dead parts; this usually takes weeks and months in its accomplishment, so that the suppuration and the fever which occasionally accompanies it debilitate the patient, and delay the final cicatrization greatly, when proper treatment is neglected. Of course we must occasionally also expect to find partial or total destruction of the gland.

Syphilitic disease of the testicle is not very infrequently bilateral and is occasionally caused by an injury. A previous epididymitis following gonorrhœa does not seem particularly to predispose to the deposition of syphilitic products, otherwise gummata would be more frequently observed, or at least make their appearance earlier in the epididymis than in the testicle; as a rule, however, just the reverse is the case.

On the other hand, the wrong idea that the *epididymis* does not become affected alone, or only in very exceptional cases, by lues, should be most energetically combated. Isolated nodular infiltrations of individual portions of the epididymis, most frequently of the head, in persons suffering with syphilis have been frequently observed by me, and found to disappear wholly or in greater part under antisyphilitic treatment; among these were also patients who had not suffered from urethritis previously, and therefore the idea of a predisposition occasioned by previous disease could not be entertained.

Diagnosis.

As syphilis of the testicle is most frequently observed in the later stages of the disease, it usually makes its appearance accompanied by older gummatous processes in other regions (the skin, the subcutaneous tissue, the nasal, oral, or pharyngeal cavity, the periosteum and the bone, in internal organs, visceral formations, the nervous

system), or there are present contemporary signs of a former lues in the shape of defects, perforations, cicatricial deformities, etc. A general enlargement of the lymphatic glands is also quite frequently present; occasionally those of the groin seem to be most deeply involved. There are, however, also cases in which the accompanying symptoms of syphilis are subordinate or altogether absent; in this case we have only the symptoms on the part of the diseased organ to go by in arriving at a diagnosis. It becomes necessary, therefore, if only briefly to mention other affections of the testicles and epididymis which could be mistaken for syphilitic disease.

A *traumatic* orchitis or epididymitis may be recognized by the history of a previous injury and of the subsequent acute development of swelling, local pain, fever, and an inflammatory redness of the skin, occasionally going on to the formation of abscess. In the course of *gonorrhœa* an acute, very painful swelling, attaining the size of a fist, may also occur; this, however, is mainly of the epididymis, and there will at the most be an exudation in the tunica vaginalis; suppuration in this form of epididymitis is rare. The scrotum is frequently the seat of an inflammatory infiltration, the spermatic cord of the same side is nearly always tender and swollen. The discharge from the urethra frequently continues or may cease for a time.

Orchitis epidemica is an acute inflammation of the testicle, which occurs not only in adolescents, but also later (though I have not observed it beyond the age of thirty). The disease is accompanied by pain and sometimes high fever, does not attack the epididymis, and ends in recovery in a few days, the testicle returning to its normal condition. Quite frequently a swelling of the parotid gland (unilateral or bilateral) coexists, when it has not preceded the testicular disease; or a parotitis epidemica (mumps) develops after the orchitis has subsided.

In *tuberculosis* the epididymis is generally first affected. There are here numerous foci of infiltration, independent of each other, some reaching the size of a walnut; these are at first firm to the touch, but become soft in a few weeks. The skin is of a bluish-red color, forming in places prominences the size of a pea or a bean, which break and give exit to pus, sometimes laudable, sometimes of a flocculent character. The path of the fistula, which is frequently tortuous, is marked by a solid cord, which leads from the original focus of infiltration to the surface of the skin. The mouth of the fistula remains open for months, and allows the draining away of small quantities of a thin pus, which occasionally contains tubercle bacilli; the latter cannot, however, always be demonstrated. From time to time the fistulous opening becomes closed, only to be torn open again at shorter or

longer intervals by the accumulated pus. The whole process does not as a rule cause great pain, but the strength of the patient is consumed by the fever, which rarely is absent of an evening, and by the long-continued suppuration. The case becomes still worse if the tuberculous process involves the testicle itself; the individual tuberculous foci are not so easily demonstrated here as in the epididymis, and there is seen at first only the general enlargement of the gland. It is only after the process has also involved the coverings and purulent matter begins to perforate the skin that the involvement of the testicle becomes manifest. The skin of the scrotum is tense over the enlarged testicle, studded with ulcers of greater or lesser size having thinned and undermined borders; the base of the ulcers is covered partly by red granulations, partly by necrotic shreds of tissue; the testicle itself is not particularly tender, and we may distinguish harder and softer parts, the latter corresponding to the purulent centres which have discharged externally. While tuberculosis of the epididymis may now and then be spontaneously cured, this result is rarely observed in tuberculosis of the testicle. On the other hand, it is not unusual to observe an advance of the tuberculous affection towards the vas deferens, the vesicula seminalis, and the prostate, and at the same time we shall often be able to demonstrate the presence of tuberculosis in other organs, especially in the lungs.

Carcinoma, when attacking the testicle, presents itself at first as a hard tumor which later on becomes softer in spots and which does not undergo contraction. If the neoplasm grows exuberantly towards the surface, it breaks down almost immediately and an extremely characteristic, crater-like cancerous ulcer (*fungus testiculi malignus*) is formed. Pain is intense as a rule; the glands of the groin and abdomen are frequently involved in the cancerous affection.

From the above description we see that syphilitic disease of the testicle is distinguished from the *traumatic* by its slower, not acutely inflammatory course. From the *gonorrhœal* form luetic orchitis is differentiated mainly by the fact that its usual seat is in the testicle, and by the more frequent absence of a swelling of the vas deferens. If we are dealing with a syphilitic affection of the epididymis alone, the infiltration is more often developed in the head. It occurs gradually, is not very tender, and never reaches the size of a blennorrhœal epididymitis. *Epidemic orchitis* is recognized by the fever, the intensity of the early symptoms, and the acute course. Although the syphilitic affection has a chronic course in common with the *tuberculous*, still the frequent seat of the latter in the epididymis, the purulent disintegration, the evidence of tubercle bacilli, and the frequent involvement of the vas deferens, the seminal vesicles, and the

prostate are sufficient for the diagnosis of tuberculosis. Syphilis and *cancer* both again very frequently have the same origin in the testicle; but the differentiation may be made on the one hand by the continuously progressing affection of the lymphatic glands which is characteristic of carcinoma, and on the other by the subsequent contraction of the testicle which is generally present in lues.

I would, however, emphatically repeat that individual symptoms alone should never decide us; therefore the diagnosis is to be made only after the symptoms present have been taken into consideration.

The Vas Deferens.

The vas deferens only very rarely becomes affected in the course of syphilis; at least the recorded cases of this affection are very few in number. I have occasionally seen nodular and only slightly tender indurations of the spermatic cord existing along with syphilitic sarcocele of the same side and gummatous ulceration of the glans. M. Zeissl has reported a case of suppurating infiltration in the parts about the vas deferens occurring in a patient with a papular syphilide. Bert observed a case in which two nodules existed on each of the two spermatic cords; on one side absorption took place under specific treatment, while the nodules on the other side broke and discharged a gummatous material.

The Seminal Vesicles.

Still less is known of syphilitic affections of the seminal vesicles. G. Lewin once found the walls of the seminal vesicles indurated; in another case a cartilaginous induration of the walls was present to such a degree that there was hardly room for the head of a pin inside.

Observations on affections of the *prostate gland* are also very few in number.

The Semen.

There cannot be any doubt whatever that the semen is also affected by the syphilitic poison; the observations of cases in which the disease was transmitted to the fœtus through the semen speak for this too plainly to admit of dispute. Up to the present time, however, we do not possess any exact information as to the manner in which this is accomplished. The most plausible theory is that according to which irritative syphilitic changes in the genital organs, especially in the testicle, bring the contagium in contact with the seminal fluid, especially with the spermatozoa, and thus transmit the disease to the fœtus, and perhaps also facilitate the infection of

the mother. It is, however, also conceivable that the contagium of syphilis is merely excreted by the generative tract without depositing any morbid products in the latter; in that case, paternal heredity would be the result merely of the mechanical admixture of the contagium with the semen.

We know that the period during which syphilis is transmissible to the fœtus is much greater than that which we usually recognize for extrauterine infection. The semen must therefore possess the property of preserving the infectious quality of the contagium for a long time; or the contagium is so altered, after syphilis has existed for a long time, that it can produce only gummatous deposits in the product of conception, but is unable to infect other individuals (see above).

It is also well known that congenitally syphilitic children with irritative lesions are more dangerous to healthy persons about them, nurses and others, than those having gummatous deposits.

From this we see that we have here to do with processes which do not cause any particular disturbance in the economy of the generative organs; we shall therefore hardly expect to discover any marked changes in the organs which elaborate the semen, even in those cases in which the father, from all the symptoms present, might be charged with being the author of the syphilitic disease of the child. The morbid changes necessarily present in such a case are very slight.

When the testicle is gravely diseased, we may also look for greater disturbances of its physiological function. The production of semen becomes less, it may even totally disappear. As, however, the destruction of these organs by syphilis does not occur until late, the decrease in the secretion of semen and complete aspermia (as well as the impotence connected with it) belong to the later stages of lues.

The Female Generative Organs.

The anatomico-physiological conditions explain sufficiently why the female genitals present a fairly extensive field for syphilitic infection. Thus we may find the *primary lesion* present in any part of the genital tract from the vulva to the mouth of the womb; the labia majora and minora, the folds of the hymen, the præputium clitoridis, the clitoris itself, and the introitus furnish most of the usual seats of the primary infection; somewhat less frequently, but still not rarely, we find infection of the vaginal portion, especially of the posterior lip of the os uteri.

Initial lesions of the vagina are most infrequently met with. If, however, an infection of the female by the virile semen is admitted,

we must also assume the possibility of an initial lesion occurring in the cavity of the uterus or in the tubes.

The External Genitals.

The external genitals of the female are also favorite points for the occurrence of *irritative syphilitic lesions*, especially of mucous patches. In the lumen of the vagina I have only rarely met with papules; they are somewhat more frequently met with on the lips of the os uteri. R. Virchow has not infrequently observed "papular swellings" on the mucous membrane of the uterus in syphilitic women; he also considered it highly probable that an "endometritis papulosa et tuberosa," which he observed post mortem in a syphilitic subject, was itself due to syphilis.

If we leave aside some unauthenticated communications of older authors (Petrus Maynardus, Antonius Benivenius, Astruc), who moreover held mercury responsible for many secondary conditions, we needs must regard *gummatous affections* of the female organs of generation as rare occurrences. They have been most frequently observed on the external genitals. They rarely occur within the vulva, though I have seen a few in this situation. In one case of gumma of the vagina, there was a tumor the size of an apple which was characterized by a peculiar obstinacy. After long-continued treatment I finally extirpated the tumor and sutured the wound; healing took place by first intention.

The Uterus and the Tubes.

Gummata of the portio vaginalis are more often encountered. It should also be remembered that the vagina may be endangered by gummata of the rectum; fistulous passages have been thus formed. We are not in possession of any authentic reports of gummata of the body of the uterus. Bouchard and Lepine each observed three gummatous nodules the size of a hazelnut in the tubes of a woman with gummata in the liver and brain.

The Ovaries.

Affections of the ovaries have been frequently demonstrated in syphilitic subjects. Cases of *diffuse* and *gummatous oöphoritis* are believed to occur. The former is more frequently recognized by its results. At autopsies of women who had not yet reached the climacteric, we find ovaries of a normal or diminished size, which are fibrous throughout, cicatricial in structure, and without Graafian follicles. In a patient, forty-three years of age, suffering with osseous pains, Lancereaux found in the neighborhood of the ovaries two tumors

(which it is true had appeared after a fall on the abdomen) which were reduced in size after the exhibition for twenty days of iodide of potassium; the tumor on the left side could hardly be made out at this time.

That affections of the ovaries and the uterus are not without effect on the development of the fœtus, goes without saying. Syphilitic affections of the uterus, which are followed by cicatricial or callous changes, are also dangerous in that this destruction of the uterine tissue may become the cause of a dystocia. Initial lesions as well as the later products of syphilis situated on the cervix uteri and on the portio vaginalis have moreover led to more or less grave obstructions during labor (Putegnat, Martinelli). F. A. Doléris has given us a minute description of these conditions.

SYPHILITIC AFFECTIONS OF THE OSSEOUS SYSTEM.

The syphilitic affections of the bones and the periosteum are of especial importance for more than one reason. In the first place it is an interesting fact that that pathological product which is peculiar to syphilis and especially characteristic of it, the gumma, was first recognized and studied in bone and periosteum; and again, the osseous system is markedly subject to this morbid process, which occasionally continues through a whole lifetime, and the alterations there occurring may be in themselves alone a source of great danger.

As we know, syphilis is next to tuberculosis that constitutional disease which most frequently leads to amyloid degeneration in important organs; but chronic suppurative processes in the bones are in themselves regarded as prominent etiological factors in the degeneration mentioned. We have already seen, furthermore, that syphilis, like every other disease which induces anæmia, causes a lymphoid change of the bone marrow, and this is all the more pronounced when disease of the bone is present. The study of syphilitic bone affections has finally acquired additional importance through the recognition during the latter part of this century of disease of the epiphyseal cartilages occurring in hereditary syphilis. Before, however, entering on a discussion of the syphilitic affections of the osseous system, we must not fail to mention that the very existence of this form of disease has been denied by some. From the very beginning of the doctrine of syphilis, there runs through it like a thread the reproach of the antimercurialists that the severe forms of lues, especially the bone diseases, are caused by mercury, this charge being strengthened by the finding of mercury in the tissues, espe-

cially in the bones. From the sixteenth century to the present day we find in the literature many recorded instances of this, but while some of these communications are made by high authorities, they are nevertheless of doubtful credit. Robert Overbeck has collected, in a large work, most of the reports concerning the deposit of metallic mercury in the bones, and has critically discussed their value. This is, however, not the place to enter upon this controversy more minutely, and we shall, in the course of this article, touch on the disturbances caused by mercury only in so far as they have some connection with our subject. While not denying absolutely the possibility that mercury may exert some influence on the osseous system, I nevertheless maintain that syphilis itself can and does cause morbid changes in the bones.

The Periosteum.

Syphilitic affections of the periosteum are of exceedingly frequent occurrence. Among them we have to differentiate a simple periostitis from one associated with gummy products.

Simple periostitis may end in various ways. The periosteum becomes thickened over one or more circumscribed portions, more rarely over larger surfaces, by a new growth deposited beneath it, which at first is intimately adherent to the periosteum and only loosely lies on the bone, but which frequently goes on to ossification and in that case seems to be moulded intimately to the bone as an osteophytic formation, or which forms a hemispherical or semioval prominence. If, in the latter case, the deposit has united with the bone, only the constriction existing at the base will point to the fact that the newly formed mass of bone has not originated from the bone, but from the periosteum, and has subsequently become welded to the bone. The neoplasm is occasionally characterized by a peculiar density, and its composition is frequently the same as that of the bone to which it is attached. These are the syphilitic products that have long been known under the name of *tophi:* "Tophacei (scilicet tumores) sunt constantes ex materia penitus lapidosa, et videntur veluti tophi ossei, vel materia illa, qua ligantur ossa fracta" (Fallopius). In other cases this ossifying periostitis syphilitica extends over large surfaces, causing marked thickening of the bone.

All these periosteal deposits may disappear up to a certain point, especially when proper treatment is employed. If absorption begins before the periosteal product has gone on to ossification, the latter may disappear entirely. On the other hand, purulent disintegration of the periosteal neoplasm will occur in badly nourished scrofulous (tuberculous) individuals when other factors (traumatism,

etc.) are added, and thus occasion is given for caries and necrosis of the upper layers.

Gummatous Periostitis.—Besides the periosteal affection just described, which may occur independently of syphilis, we very frequently meet with elastic, soft, periosteal swellings which are peculiar to syphilis, viz., gummata. As the affection here is also caused by inflammatory irritation of the periosteum, only with the difference that the product of inflammation takes on the character of a gumma —a lesion which is encountered also in other tissues—we may very well speak of a gummatous periostitis. Here we meet with circumscribed hemispherical or flattened prominences which are sometimes hard, sometimes rather of a mucoid consistence, soft and elastic, and giving the impression of fluctuation. The gummatous product arises especially from the inner surface of the periosteum, but involves at the same time the bone, in which we find a depression corresponding to the gummatous swelling, and gummatous plugs are also seen passing into the Haversian canals. The periosteal gumma thus seems also in part to be embedded in the bone from the fact that the gummatous product has apparently eroded this tissue. But alongside of this destruction of bone we find in the parts adjacent to the base and the periphery of the gumma, a sclerosis and hyperostosis which frequently reach a high degree.

If the periosteal gumma goes on to absorption, which quite frequently happens and is usually accomplished by fatty degeneration, the part may look sunken. This may be due to the fact that the overlying skin has been stretched and thinned by the pressure; but even when no such change has occurred this depression will still be found because of the loss of substance in the underlying bone. The wall occasioned by the formation of bone at the periphery will remain for a long while and serve as a characteristic mark of the depression left after absorption of a periosteal gumma. In time, however, even this bony formation will become absorbed.

Flat bones may thus readily become perforated, if periosteal gummata are present in corresponding places on both surfaces. As these pit-like indentations and perforations occur without the formation of pus, so to speak in a dry way, the condition has been called by Virchow "caries sicca."

In some cases, however, the gumma of the periosteum becomes liquefied and leads on the one hand to superficial caries and necrosis, on the other to an absorption of the overlying soft tissues, which are frequently the seat at the same time of a gummatous infiltration; in this way is formed a fistulous opening leading to carious and necrotic bone. If the process does not extend the superficial layers of bone

will be thrown off, and there will result an osseous cicatrix into which the cicatrized soft parts are tensely drawn.

That a periosteal gumma may become ossified, that therefore the gummatous periostitis may be an ossifying one, is not probable. The elements constituting the gummata are so characteristically frail that any higher degree of organization can probably be excluded. The gumma may possibly excite a new formation of connective tissue, which becomes a callosity (as in the liver, lung, etc.), or an osseous new formation, but it is not very likely that it can itself become transformed into connective tissue or bone. For this reason we believe that gummatous periostitis progresses only in the direction of absorption or ulceration.

The Bones.

As in the case of the periosteum so in that of the bones and marrow, we distinguish between a *simple* (syphilitic) *ostitis* or *osteomyelitis*, which is analogous to the non-specific process, and a *gummatous ostitis* or *osteomyelitis*, in which the inflammatory neoplasm assumes the character of the gumma. This lesion is, as we have frequently said, peculiar to syphilis.

Ostitis simplex in the majority of cases induces thickening of the bone. This thickening, however, is not always permanent, but on the contrary absorption usually occurs after the osseous process has run its course, and the loss of bone tissue resulting therefrom is not confined to the osseous deposits alone, but also involves the healthy portions, so that the bone may finally even become osteoporotic. The ostitis, and especially the osteomyelitis, may, however, terminate in the usual way, that is to say, in caries or necrosis.

As already mentioned, the affection in which an accumulation of cells is deposited within the bone or its medullary cavity, the gumma, is characteristic of syphilis. Since the times of Dittrich and Ricord, but few cases of central gummata of the bones have been recorded in literature; but the researches of Chiari teach that Lancereaux was perfectly correct in assuming that this was simply due to the infrequency of anatomical exploration in this direction. The gummy deposit makes its appearance within the bone as a rule in small foci the size of a pin's head to that of a nut, which are at times of a rounded form, at other times having offshoots. The growth of the individual focus is always accompanied by rarefaction and absorption of the bony tissue, while the part surrounding the gumma is indurated.

Under favorable circumstances, that is to say when the gummy

deposits are not very large, even if numerous, absorption is the rule. The parts first attacked become osteoporotic, and as there is sclerosis of the parts surrounding the gummata, we shall find both hypertrophic and atrophic areas of bone after the process has run its course.

If absorption is incomplete, however, a portion of the gumma will remain behind as a caseous mass. The larger the gummatous deposit, the more likely is this to happen, because in this case there will be present a disproportion between the absorbing surface and the mass to be absorbed. Within the bone itself the power of absorption will be still more diminished by the fact that the gummy mass induces a sclerosis of the bone in its vicinity.

The gummy infiltrations quite frequently occupy the bony tissue in such a manner that they surround a portion of bone in the form of an island. The nutrition of such a bony island is cut off by the intervening gummatous matter and the part becomes necrotic. Smaller sequestra, and occasionally some larger ones, are apparently destroyed by the erosion caused by the gummata; large sequestra will have to be removed. The portions of bone which have become necrotic after a gummatous ostitis are markedly characterized by the fact that they are traversed in many directions by small channels and holes, as though worm-eaten. The reason of this is that the gummatous deposits which are the cause of the necrosis also penetrate the portion doomed to necrosis and so impress the marks of the past disease upon the sequestra. Necrotic parts remaining after a non-syphilitic (traumatic, scrofulous) ostitis have a smooth surface as a rule and do not present any marked changes. The involucrum in gummatous ostitis is also perfectly characteristic; the walls of the cavity present marked induration, and the opening or mouth of the involucrum is surrounded by a bony wall. After the sequestrum has been expelled the cavity is very imperfectly filled up; the defect is consequently very manifest, and is still more distinctly marked by the bony wall surrounding it.

We have as little reason to assume an ossification of the gummatous infiltration in ostitis as in periostitis.

We have yet to study syphilitic affections of the bones, the starting-point of which lies in the soft parts which cover them. Chronic processes, which are mainly situated in the skin, may also react on the bones lying below; I need only to mention *favus*. The underlying bone is either stimulated by the skin disease to produce vegetations, or the parts under consideration become atrophic. The involvement of the bone is, however, much clearer when the soft parts which cover it go on to ulceration, denuding the bone as disintegra-

tion progresses, and causing necrosis or caries, if only superficially. From this point of view the cutaneous and subcutaneous as well as the mucous and submucous gummata must be considered, especially when they are situated at no great distance from the bone. When such gummata ulcerate, denudation and caries threaten. The inner bones of the nasal cavity are in especial danger. We have already mentioned the fact that entire bones may be destroyed in this way.

In addition to the affections described so far we have yet to touch on a form of atrophy which may affect the whole osseous system or only single bones. This is probably not directly connected with the syphilitic process, yet it deserves our attention as it has its remote origin, at least, only in a previous or still present lues.

When a syphilitic infection is of long duration, lowering the nutrition of the entire organism, a cachexia is produced just as in other chronic affections, and in the course of this a constitutional depravity is formed, which occasionally also extends to the bones. The latter lose their firmness and elasticity, the least forcible exertion is sufficient to break them; in short they are affected with *osteopsathyrosis*, or fragility of the bones. This fragilitas ossium affects a great number of bones, especially of the long bones. According to the researches of M. Charay, who found in seemingly healthy bones of syphilitic subjects a diminished power of resistance (even as much as fifty per cent.) to bending, the fragility of the bones must be referred to a marked decrease of fluoride of calcium.

Carl Rokitansky mentions as in all probability of syphilitic origin a peculiar thinning, leading here and there to perforation, which occurs as a (symmetrical) atrophy of both parietal bones and sometimes also of the occipital.

We have also been for some time aware that bones which have been made useless by ankylosis or as the result of paralysis become abnormally fragile. Thus it is that spontaneous fractures occasionally occur in patients suffering from tabes and from mental disease. And as now syphilis may cause permanent affections of the brain and spinal cord, we may expect to find atrophic conditions of the skeleton in these affections analogous to those that occur in peripheral and central disease of the nervous system, in which syphilis is not an etiological factor.

Symptoms.

Before entering upon a discussion of the symptoms we must first mention that the grouping employed by us is not always observed clinically, and that we are not able always to differentiate the affections of the periosteum and those of the bone.

The Periosteum

In the common form of (purely irritative) periostitis, a painful flat swelling occurs, which, when the bone is situated superficially enough, is recognized as diffuse and of greater or less extent. The general condition is, however, not impaired, even in an extensive periostitis, to such a degree as is usually the case in periosteal inflammations; and for this reason the patient is as a rule only rarely debarred from following his occupation.

It is sometimes remarkable how patients with an extensive periostitis of the tibia, in spite of its painfulness, are able to move about freely, or those with cranial periostitis, in spite of the painful thickening of the periosteum of the skull, are rarely compelled to interrupt their occupation. As has been mentioned, the inflammation has always been found to affect the inner surface of the periosteum. It is possible, however, that under certain circumstances the superficial external layer may be mainly affected.

It may be stated in general that a periostitis in which there is no increase of the swelling, after the disease has existed for a short time, but rather a decrease of pain, will, under proper management, in all probability end in absorption.

If the pains decrease without a decrease at the same time of the swelling, or if an increase of the periosteal swelling is evident while the pain decreases, we may predict an issue in ossification, even when clinically we are as yet unable to demonstrate the beginnings of such a change in the periosteal product.

It is only after the disease has existed a few weeks or months that we shall find in parts accessible to physical examination either an extensive area of thickening or multiple small excrescences which are sometimes rounded, sometimes pointed, or isolated hemispherical or semioval bony prominences. In consequence of these changes disturbances are engendered which are dependent in part on the increased weight of the bones, in part on the pressure which the diseased products exert on the neighboring vessels, nerves, and other tissues.

It is characteristic that these various areas of periosteal ossification may still be absorbed, up to a certain degree. The thickened bone decreases more and more in size and becomes porous, the bony points and excrescences become rounder and flatter. The feeling of weight then gradually disappears, and also other symptoms produced by pressure are no longer felt. Those cases are very remarkable, in which the ossifying inflammation of the periosteum approaches the insertions of muscles, and in which the ossification also

extends farther, even to the substance of the muscles, so that in a few recorded cases entire muscles have become ossified. This affection, known by the name of *myositis ossificans*, which occasionally makes its appearance after great exertion (at other times again—*myositis ossificans progressiva*—as a result of a disease of the central nervous system), seems also frequently to be due to syphilis. Many other still unknown factors, however, may be concerned. Thus C. Hawkins mentions the case of an individual who was eminently predisposed to those ossifications, in whom simple pressure by the finger was sufficient to cause ossification of the muscles. This disappeared, however, after the administration of iodide of potassium, reappearing again when the former cause was repeated, and again disappearing on the administration of the same drug.

If periostitis goes on to *suppuration*, pain is severe only when the inflammation runs an acute course. The periosteal inflammatory swelling is then painful and exquisitely tender on pressure. The skin, which is involved in the inflammation later on, also becomes swollen through collateral œdema, is reddened, but takes on a bluish color and becomes thinned where the convexity is greatest. After the pus has once perforated the periosteum, the pain suddenly decreases, but only for a short time; it is totally abolished when the skin also gives way in one or more thinned places and the pus is thus enabled to make its exit. If we now pass a probe through one of the openings in the skin, which corresponds to the periosteal perforation, the rough surface of the bone is easily reached, and if a proper curve is given to the probe, may be explored in its whole extent as far as the periosteum has been raised by the pus. If the pus is enabled to flow off in its own channels or is led away by artificial drainage, the periosteum which has previously been raised becomes again adherent throughout its greater part by means of granulation. In those parts, however, in which the periosteum has been destroyed or goes on to suppuration granulations spring from the bone, sometimes after previous exfoliation of one or more of the outer layers, and furnish the material for a cicatrix, with which, after healing is completed, the cicatrix of the soft parts and of the skin becomes intimately adherent or attached by a longer or shorter cicatricial band.

A suppurative periositis, however, frequently runs a slow course. In that case reaction is slight, pain is insignificant, and the pus does not so readily gravitate to the dependent parts forming a cold abscess or gravity abscess. Cold abscesses in syphilitic periostitis do not always perforate externally, and the contained pus, under proper treatment, is more frequently absorbed than is usual in scrofulous (tuberculous) abscesses.

When a *gummatous periostitis* is present, we find one or more circumscribed infiltrations, the size of a chestnut or larger, accompanied frequently by great pain. These are firm in the beginning, but after a while when softening and liquefaction of the infiltration have occurred, the sensation of fluctuation becomes prominent. The skin is puffed out by the periosteal gumma if the latter is situated superficially, but retains its normal color for a long time. If the gumma goes on to absorption, which is to be expected in most cases, the skin becomes only slightly discolored. If the gummatous infiltration breaks down, however, the skin will also be markedly discolored and becomes thinned. It finally gives way at the most prominent point and discharges a slimy, ropy fluid, more or less turbid from admixture of pus and blood, in which a few shreds of necrotic tissue may be found. The liquefaction and disintegration of the gumma proceed from its centre, and it may happen, therefore, that the swelling does not collapse in spite of the perforation, for the reason that the marginal portion of the gummatous infiltration has not yet become liquefied. We shall also observe an increased deepening and enlargement of the ulcerating cavity, so long as any disintegrating gummatous infiltration remains. Only after the peripheral portion of the gumma is destroyed will the walls of the ulcerating cavity collapse; this diminishes now in so remarkably rapid a manner that only a few granulations are necessary to fill it out and permanently cicatrize it. In nearly all cases of periosteal gummata we find the bone also diseased in the parts corresponding to the periosteal gumma, and it participates in the absorption as well as the disintegration of the gumma. We shall therefore find nearly without exception, no matter whether the morbid product has disappeared by absorption or by ulceration, a pit-like depression in the bone at a part corresponding to the seat of the periosteal gumma. On the other hand, however, the gummatous affection has excited a sclerosing ostitis in its immediate neighborhood, and this is accompanied by bone formation. The depressions left behind after the periostitis has healed, therefore always appear surrounded by a more or less broad bony wall.

The Bones.

It is not always easy for the clinician, even in periosteal affections, to determine at once whether he is dealing with an irritative periostitis, or with a gummatous process, and a minute differentiation in case of an affection of the bone or its marrow is utterly impossible. We shall, therefore, speak of ostitis and osteomyelitis only in a general way, although we may say that gummatous changes

occur probably much more frequently than the purely inflammatory forms.

The recognition of a beginning ostitis or osteomyelitis is surrounded by difficulties. The morbid process, which is generally of slow course, occasions only a dull pain in the deeper parts, which, however, greatly increases in the further course of the disease, and is accompanied by marked exacerbations in the evening. It is seldom that the pain is of such an intensity that functional disturbances of the diseased bone are induced. The patient as a rule does not feel especially ill. Fever is slight or absent entirely. Objective changes in the bones or soft parts, even in cases in which the affected bone is superficial, are usually tardy in making their appearance. But just this continuation and even increase of pain down in the interior of the bone, as well as the absence of demonstrable morbid changes in the periosteum and the soft parts, will leave no doubt in our minds as to the seat of the disease. The subsequent symptoms will differ according to the issue of the disease. If the ostitis leads to sclerosis a sensation of heaviness in the affected bones will be added to the original symptoms of indistinct character. When, however, this induration leads to a narrowing of foramina, canals, or even cavities, and thus to a compression of the contents of the same, to the otherwise simple group of symptoms will be added the pressure symptoms in the parts encroached upon.

When sclerosis attacks one of the large bones and marked thickening exists, the affected extremity will naturally appear heavier to the patient, and its functions may also occasionally be interfered with. But even when very pronounced sclerosis is present, the troublesome symptoms the patient experiences will leave him after a time, not only because he becomes used to them, but because the diseased bones in reality also become lighter and the foramina wider, as the newly deposited osseous material is again in part absorbed. In rare cases, however, absorption, as has been mentioned above, sometimes exceeds the measure of the hyperplasia, and then osteoporosis, and with a still greater degree of absorption, fragility of the bones will result.

The issue of an ostitis simplex in a bone abscess is, as has been said, rare.

Gummatous ostitis and *osteomyelitis* may occasionally be accompanied, it is true, with much pain, but it may also unquestionably run its course without any symptoms whatever. In the cases observed by Chiari, osteocopic pains could be positively determined in only one. It is therefore not improbable that syphilitic ostitis, especially when it has ended in absorption, has often occasioned such

slight disturbances that it has run its entire course without a suspicion of its presence on the part of the patient.

Not infrequently I have been able by means of percussion to determine quite accurately the location of the disease focus in the bone and to reveal the existence of tender spots in the tibia, the calvaria, or other bones, even when no complaint had previously been made by the patient, and have consequently felt myself justified in assuming the existence of ostitic changes in these parts. A gummatous ostitis is, however, frequently enough ushered in by a pain localized in certain parts occurring after exertion or in the form of exacerbations at night. When the periosteum and the surrounding soft parts are involved, these parts are welded together into one resistant tumor. The gummatous infiltration sometimes occasions, when its seat is central, a thinning of the peripheral parts until a bony shell only is left, which becomes distended by the pressure of the enclosed product continually enlarging, and crepitates when pressure is made (*spina ventosa*); or osteoporosis is developed, so that a bone of this kind yields to a very slight force. Doubtless many so-called spontaneous fractures may be due to an underlying ostitis gummosa.

If absorption of the gummatous infiltration takes place, any morbid symptoms which may have been present will gradually disappear. We must not forget, however, that a rarefaction remains behind which alternates with areas of greater density in the neighborhood of the originally affected foci. If the rarefaction is extensive, the bone will retain a certain fragility even after the gumma has healed; we are, therefore, liable to meet with spontaneous fractures even in this stage. The loss of bone which has been initiated by the gummatous infiltration may, however, also show itself as a shortening or even entire destruction of a bone, as we may observe in the phalanges, thus producing a kind of mutilation.

When gummatous ostitis leads to necrosis, the suppuration accompanying the inflammation of demarcation will cause pain according to the degree of tenseness present. Obstruction to the flow of pus may, however, also dispose to erysipelas and inflammation of the deeper structures, and so produce manifold disturbances. When the pus has free drainage, which is sometimes facilitated by ulceration of the soft parts, the graver symptoms usually disappear, and only the suppuration remains copious, the pus having a foul odor, until the bone is completely exfoliated and reaches the surface. Only now we may expect healing, generally accompanied by adhesions of the soft parts to the bone. It should be mentioned here that smaller pieces of bone are consumed, eroded by the neighboring granulation cells, and are seemingly dissolved, while larger sequestra present the

worm-eaten appearance already described. Flat bones become thinned by this process or even perforated, while the long bones lose their firmness, and ocasionally are fractured by very slight causes.

The affections of the bones and periosteum here discussed have been looked upon for some time as the most certain sign of the entrance of syphilis into its "tertiary stage." We have, however, repeatedly called attention to the fact, and again point out, that there are really no sharply defined boundaries between the several periods of syphilis. Experience has shown that even involvement of the osseous system does not always point to a lues of long standing, as affections of the bone and the periosteum frequently enough make their appearance when the disease has existed only a short time. Suchanek in a work worthy of perusal places affections of the bones among the first symptoms of the constitutional disease; and there existed, during the course of the initial lesion, in skin, mucous membrane, and bony syphilis a proportion of 18, 12, 7. We observe here plainly, as well as in syphilis in general, that as a rule lighter forms make their appearance in the first period of the constitutional disease, while graver forms belong to a later stage. However, in this direction even we cannot speak of a generally accepted rule for the reason that a gummatous ostitis may develop even during the first months of infection. Thus I have observed tophi of the frontal bone and of the tibia among the first signs of constitutional syphilis. In a case mentioned by E. Soloweitschik, a widely diffused affection of the bones of the skull was present three months after infection.

The original idea regarding the order followed by the diseases of the tissues also cannot be maintained. Although the signs of the constitutional disease are first observed on the skin and mucous membranes as a rule, we nevertheless learn from an unbiassed clinical experience that syphilitic affections of the bones occasionally usher in the constitutional symptoms.

We shall, therefore, at different periods in the course of syphilis find diseased bones, and besides meet with various other symptoms of the affection. It may, however, much more frequently happen that syphilis of the bones occurs in the absence of recent signs of lues in other organs. It is in the osseous system especially that the disease may occur most frequently alone, and indeed it exists alone here even more frequently than it does in the skin.

If we consider the individual bones, we find that not one presents marked immunity from the syphilitic process; Dittrich even found a caries and necrosis of the hyoid bone in a female day-laborer, thirty-one years of age, who presented also other symptoms of syphilis. It is, however, a fact that some bones as compared with others are espe-

cially liable to be attacked by the disease. The bones of the skull are quite frequently attacked in the course of syphilis, and of these especially the frontal bone, the parietal bones, the bones of the nasal skeleton, and of the hard palate. On the other hand, affections of the occipital and temporal bones are more rare.

Affections of the long bones are also of frequent occurrence, and those of the legs and forearms seem to be more frequently involved than the femur and humerus. The clavicle and secondarily the ribs are very often involved in the syphilitic process, while the vertebræ, as well as the short bones as a whole, are somewhat less frequently attacked. Of the long bones it is again interesting that their diaphyses are more frequently affected in the course of syphilis than their epiphyses. In individual cases, however, the articular surfaces also become the seat of gummata, and in consequence the joint is finally also threatened.

The disease only rarely affects the whole bone; as a rule the process is localized to a few foci which, at the same time or successively, develop in one or more portions of the bone. What the cause of this predilection is, we do not know with certainty. The general opinion which, on the whole, is entitled to a certain amount of respect, in view of analogous observations on the skin and the mucous membranes, is that those bony parts which are more exposed to external injury are also more disposed to syphilitic affections, and as a matter of fact, the bones situated superficially (frontal bone, tibia, clavicle, etc.) are much more frequently attacked than the others. In taking the history we frequently find that the patient refers the disease to some injury, but such statements are as a rule so unreliable that they are not generally to be taken into consideration. Nevertheless it is possible that not a few cases may arise in this manner.

Positive data on this point are had when known injuries have acted on the bones of a syphilitic subject and led to fractures. But even in these cases the experiences of different observers are not in accord. Formerly the view was quite generally held that fractures of the bones (as also wounds of the soft parts) in syphilitic subjects would heal only slowly; at the present time such apprehension is looked upon by the majority as baseless or at least exaggerated, and undoubtedly the truth lies between the two opinions. As we frequently enough see injuries to the soft parts in patients with florid syphilis at one time heal without trouble, at another time, however, serve to prepare the soil for a new syphilitic product, so we have in some cases of fracture to apprehend a retardation of the healing process, in spite of the frequently normal formation of callus on the bones of syphilitic subjects. The failure to unite is probably due to the pres-

ence of a fresh deposit of gumma at the point of fracture. But there are also many cases on record in which properly treated fractures of the bones in syphilitics showed only an imperfect formation of callus, and in which finally a bony union was obtained only after the institution of antiluetic treatment.

As we have already frequently said, the use of mercury has at every period in the history of syphilis been made answerable for affections of the bones occurring in the course of this disease. To the extent expressed, the accusation is certainly not justified; for from the times of Ulrich v. Hutten to the present day we are in possession of authentic cases, which teach us that bony affections have occurred in patients who had never taken mercury, and occasionally such cases have pursued an extremely stubborn course. The more moderate of the antimercurialists, therefore, confine their accusation to the statement that the administration of mercurial preparations merely favors the appearance of syphilitic bone affections. The careless administration of mercury may, as we shall later discuss more minutely, produces changes in the bony system, but these are represented either by a fragility as the result of a probable mercurial dyscrasia* or by a necrosis of the jaw-bone after a severe case of stomatitis mercurialis. Diseases of the bone, however, which can be compared to syphilitic periostitis and ostitis have not been observed in pure hydrargyrosis. It is nevertheless possible that the bones may acquire a greater disposition to syphilitic processes as a result of the administration of mercury in over-large doses.

Syphilitic affections of the periosteum and bones are only rarely of short duration, and then chiefly in periostitis occurring soon after infection. I have repeatedly observed the absorption of periosteal swellings, which had made their appearance together with other syphilitic symptoms, within a few days and occasionally without any antisyphilitic treatment whatever. The usual course, however, is that these processes, especially when they are located in the bones, drag along for weeks and months or even years. The affections which

* T. L. Prevost, with the cooperation of A. Eternod and G. Frutiger, studied the effects of the subcutaneous administration of mercurial salts in the animal, as the result of a case of poisoning in man. One of the first symptoms observed was intestinal hyperæmia (inflammation, ecchymoses) of the intestinal tract; very soon albuminuria also made its appearance, and calcification of the convoluted uriniferous tubules. With the increase of the calcification in the kidneys, a diminution of the quantity of urine, which, however, always contained albumin, went hand in hand. The lime in the kidney was derived from the bones; and the loss of lime from the latter might be so excessive as even to cause a separation of the epiphyses. Salkowsky observed diabetes, associated with the above-mentioned changes in the intestinal canal, after mercurialization.

lead to thickening and condensation of the bone or to caries and necrosis are characterized especially by their extraordinarily slow course. We must not, however, overlook the possibility of the osseous manifestations being especially prolonged by the repeated and successive formation of gummatous foci.

It is characteristic of syphilitic bone and periosteal affections that these are not always very painful, and in such cases grave functional disturbances only rarely make their appearance. Although we may surmise that the pain is dependent on the size of the exudation, it is still a matter of observation that manifest swellings are not always accompanied by pain, and also that great tenderness is frequently observed in bones which do not show any signs of a swelling. Suchanek has written an instructive work in this connection. Among 115 patients in Waller's clinic there were observed in 25 cases only subjective, in 24 both subjective and objective, and in 66 only objective symptoms.

The quality of the pain is furthermore not characteristic of syphilis; this is sometimes described as boring, beating, or sawing, at others as tearing, dragging, or simulating some other sensation. The idea of the nocturnal character of syphilitic bone pains has gained much ground among physicians. It is true that the pain is much increased during the night, but it should be emphasized that something similar is also observed in other chronic exudative changes.

Other symptoms of syphilis in the periosteum and bones are influenced by the locality. As already pointed out, the *bones of the skull* are very frequently affected in the course of syphilis; so long, however, as the disease process is confined to the bones alone, grave results are rarely to be expected. This, however, is partly dependent on the kind and extent of the process, partly on its seat. Periosteal swellings situated on the external surface of the bone as a rule cause only local disturbances, but when the tophus involves the inner surface it may become dangerous. This was what occurred in the case of Boys de Loury, in which a large tumor of the bones of the head had grown inwards and compressed the brain. At first the patient, a woman, complained of pain in the arms and legs, then of headache; during the last period of her life, the feeling as though a heavy weight compressed the head was prominent. We need not always abandon hope in cases of this kind, for many instances are on record in which syphilitics suffering from cerebral symptoms, caused by exostoses of the bones of the skull, have been relieved not only of the cerebral symptoms but also of the exostoses which were their cause. Gummatous ostitis ending in necrosis must be looked upon as the gravest process. Extensive affections of the skull, strange to

say, also occasionally run a latent course, so that the gummatous affection of the bone is only discovered at the autopsy. In general, however, the soft parts are destroyed sometimes to a slight and sometimes to a large extent and the bone is laid bare as a blackened mass. The course of this process is an extraordinarily slow one. If the necrosis involves the whole thickness of the bone, large holes are frequently left in the skull. It is very serious and alarming to see, after removing the necrotic plate of bone, the broad pulsating cerebral surface covered only by the meninges. Even great defects have, however, been known to heal. A firm cicatricial tissue is formed and becomes intimately adherent, partly to the meninges, partly to the bone and borders of the soft parts. The cerebral pulsations are still, although in a less degree, communicated to this tough cicatrix. As time goes on contraction of the cicatricial tissue occurs, so that the skull becomes more and more flattened at this point.

In spite of their long duration these cases of syphilitic necrosis not very infrequently end favorably, so that we shall do well in most cases, when dangerous symptoms are absent, not to interfere at all, and to allow the sequestrum to be thrown off without assistance. I remember one patient who had a syphilitic necrosis of the frontal bone for years; he refused all medical assistance and seemed to be none the worse for the necrosis. Another patient, a woman, had visited several hospitals on account of a necrosis of the same bone, but as no one attempted any radical interference, deeming it wiser to allow the bone to be thrown off of its own accord, she finally went to her native place, where nearly one-half of the frontal bone was finally thrown off. This patient visited my clinic with the bone in her pocket, to undergo treatment for the ulcerations which had exposed the meninges over a wide area. Defects of this kind in the bones of the skull are only very rarely filled with bony material.

Necrosis of the bones of the skull in which the inflammatory process extends to the meninges, producing grave cerebral symptoms, are to be very seriously considered. Syphilitic tumors of the skull which exert pressure on the brain are just as dangerous. A fatal issue is not rare in these cases; or else various forms of paralysis, epilepsy, and even mental disturbances may result.

In cases of this kind the timely removal of the necrotic portion is frequently followed by the most salutary results, as we learn from an observation of Hutchinson, in which in the course of a syphilitic necrosis of the right side of the forehead convulsions of the left side of the body and pain in the back of the head, on the left side, made their appearance. After the sequestrum had been removed a large quantity of pus was discharged and the patient gradually improved.

Occasionally a formidable operation is demanded for the patient's relief.

Fortunately the syphilitic process most frequently affects the top of the skull, a locality which is quite favorable for its spontaneous cure, as also for therapeutic measures.

Syphilitic ostitis and periostitis of the *orbital bones* are not, it is true, frequently met with, but are entitled to notice on account of the variety of symptoms which they may cause. The affection is very easily demonstrated at the edge of the orbit. Occasionally a gummatous infiltration of the cellular tissue accompanies this periostitis, which involves the lid and renders the latter immovable. Gummata of the bone and periosteum situated deeper in the orbit may also be felt by the finger pressed between the bulb and orbital wall; when the infiltration is more extensive there will be a corresponding displacement of the eyeball. The further the gumma is situated towards the back, the more difficult is it to make a positive diagnosis. This can then be gathered only from the symptoms of diminished space, viz., protrusion and rigid immobility of the eyeball. Occasionally the pain is excessive, independent of the seat of the affection, and may even imitate a severe neuralgia (F. Weinlechner). In individual cases the eye muscles, the optic nerve, or even the eye itself may become involved, or, in the case of breaking down, a fatal meningitis (Ferdinand Schott, Soloweitschick) may arise, if perforation does not occur externally as in a case reported by R. Campana. Cases which are recognized in time and properly treated run a favorable course as a rule, although in some instances a very slow one.

Syphilitic affections of the *base of the skull*, which occasionally extend from the nasal or the pharyngeal cavity, do not occur very frequently. Their course is frequently unfavorable on account of the difficulty of reaching the seat of the trouble, although necrosed portions may here also be spontaneously expelled through the nose and pharynx.

Syphilitic affections of the *temporal bone* have been observed less frequently than any others.

Of the facial bones, those of the *nasal cavity* and the *upper jaw* are quite frequently attacked by the syphilitic process. I have frequently seen affections of the *zygomatic arch*. I once observed a case of gummatous ostitis of the frontal process of the upper jaw which in its beginning had caused an overflow of tears through compression of the tear duct; in another case a necrosis of the lacrymal canal had occurred.

Syphilitic disease of the spinal column was recognized by John Hunter. Affections of the *cervical spine* seem to occur most fre-

quently. In a child who had acquired syphilis I noted, some time after the primary infection, tenderness of the cervical spine and a rigid position of the head; on the administration of iodide of potassium this condition disappeared in a few weeks.

In a man thirty-four years of age, a periosteal enlargement developed on the anterior surface of the cervical spine, to the right of the median line three-quarters of a year after infection; there were also other evident signs of syphilis. The enlargement could be plainly seen and felt to the right of the posterior pharyngeal wall. It was tender to the touch, but the mucous membrane covering it, as well as the muscular layer, presented no change. The median spinal processes were tender on pressure. There was much tenderness experienced in the cervical spinal column when the head was suddenly pressed down upon the spine; movement was also restrained.

In the case of a man, thirty-two years of age, who had been infected eight years before, I was able by inspection through the mouth to demonstrate a cavity over 2 cm. deep in the roughened bone on the left half of the cervical spine, following a gummatous ostitis (situated, as I surmised, at the level of the fourth or fifth vertebra). Gummata were also present on the skull, the hard palate, and some of the long bones, and there was difficulty in moving the neck. When large portions of the spinal vertebræ are destroyed, the spinal column will be flexed anteriorly. In this manner I have observed a kyphosis after a spondylitis of the cervical spine had run its course, in a woman forty years of age, whose genitals were covered with cicatrices. The head, which was inclined to the right shoulder, was able to execute only slight nodding motions; the mouth, whose alveloar processes and teeth were directed forwards, could be opened only to a very slight extent, so that it was impossible to inspect her throat; the nose, the septum of which was defective, contained gummatous infiltrations. The probe revealed necrosis and perforation of the hard palate. On the left, between the spinous and transverse processes of the upper cervical vertebræ, a knuckle of bone protruded which cemented the vertebræ together. Disease of the vertebral arches may cause concomitant affections of the nerve roots, the meninges, and the medulla; while disease foci of the transverse processes may become dangerous by causing erosion of the vertebral artery with fatal hemorrhage. Observations on syphilitic affections of the *dorsal* and *lumbar spine* are less frequent.

As to the rest of the skeleton, the *thorax* and the *extremities*, what has already been said in a general way of the syphilitic bone diseases may be applied to them. A few affections of the hands and feet only present certain peculiarities which entitle them to special mention.

Affections of these parts have been observed for a long time, but there was apparently no incentive to specify them as something peculiar by a special nomenclature. This may be seen from a paper read by Dr. Robert Williams before the Royal College of Physicians in the year 1834 on two cases belonging to this category. As, however, affections of the fingers in general were designated as panaritia, Nélaton was led to name an affection of these parts caused by lues "syphilitic panaritium"; A. Lücke called the same affection "dactylitis syphilitica." Since then observations regarding these have been published by O. Risel, R. Bergh, Heyfelder, Bulkley, G. Lewin, and others.

Dactylitis syphilitica frequently enough begins with an affection of the soft parts (fascia, tendons, and tendon sheaths), later on involving also the bone. Karl Koch is therefore correct when he recommends the addition to the term dactylitis syphilitica the qualifying words, "cutanea (subcutanea)," "periostealis," "ossea," and "articularis," to which I would add "tendovaginalis."

When the affection begins in the phalangeal bones, it seems to involve very early not only the periosteum, but also all the soft parts of the finger. We accordingly find one or another phalanx, or perhaps several, enlarged to twice the normal size and over, puffed up, and covered by a shining, smooth, bluish-white skin, which does not seem to be movable over the subjacent parts. Although the bone cannot be plainly felt through this puffy mass, we are nevertheless able to demonstrate its increase in thickness. This enlargement is due to a periostitis or to a central ostitis causing a swelling of the bony cortex. When strong pressure is employed we find that the bone in the latter case consists only of a much thinned, easily ruptured shell. At other times, again, the skin is pierced by one or more granulating openings the size of a pea, through which necrotic bone may be felt. In the further course of the disease a portion of the phalanx or the entire bone is destroyed by necrosis, or it is consumed gradually and cast off in the discharge from the granulation wound. The swelling of the finger gradually subsides, and after the cure is perfected we find a thinning and shortening of the phalanx corresponding to the loss of bone. In rare cases we shall, however, also find a marked new formation of bone and as a result an elongation of the finger.

The terminal phalanges, when affected, enlarge usually in the form of a drumstick, resembling Hippocratic fingers, such as are found in chronic heart and lung diseases.

When a neighboring joint becomes involved destruction of the ligamentous apparatus takes place, resulting in a loose joint, or we

get ankylosis in consequence of adhesions and contractions of the new fibrous tissue.

The whole course of the disease is extremely slow and but slightly painful. It is not developed as a rule until some time has elapsed after infection, but in hereditary lues it commonly appears during the first few years. The affection on the whole is more frequently observed in the phalanges of the fingers than in those of the toes. The same form of the affection may appear on the metacarpus and metatarsus. An ulcer bordered by an epidermic callosity on the sole of the foot (resembling perforating ulcer of the foot) may occur as a result of syphilis attacking bursa, tendons, and joints, and this in its further course leads to periostitis and ostitis and consequent necrosis of the bone.

Diagnosis.

It is not easy to summarize the symptoms which are useful in the diagnosis of syphilis of the bone; the reader is therefore referred to what has been previously said of this affection. We will only mention that when the morbid process affects only a single part, we must try to discover whether or not some injury has occurred previously which may directly or indirectly have irritated the bone.

Workingmen who are subjected to the vapor of phosphorus are apt to be attacked by necrosis of the jaw. A *phosphorous necrosis* may, it is true, also extend to the frontal bone and the zygomatic arch, but the affection will have first attacked the jaw-bone.

Ulcerations of the mucous membrane, and also baring of the bone and necrosis, may follow the use of *mercurial preparations*. This affection of the bone is, however, characterized by a total aplasia. This loss of productive power is also found in chronic hydrargyrosis, in which we meet with atrophy of the bone, and also with a general atrophy and marasmus.

In contrast with this, the form of ostitis which is liable to attack *turners of mother-of-pearl*, during the age of puberty, is characterized by a marked hyperplasia. The thickening is generally found in the long bones and appears first at one end of a diaphysis, spreading towards the centre and suddenly ceasing towards the epiphysis (Englisch, C. Gussenbauer, Otto Weiss). Resolution is the rule in this disease, an issue in necrosis being hardly ever met with.

Multiplicity of the bone affection is moreover frequently seen in syphilis, and from this alone traumatic causes may be excluded. However, a *necrosis disseminata* (Blasius) may occur from concussion. As, however, only dyscrasiæ (scrofula, syphilis) as a rule present like

symptoms, we will study more closely the more prominent differences between syphilis and *scrofula* (*tuberculosis*).

Experience has taught us that affections of the bones due to scrofula (tuberculosis) much more frequently lead to caries, and that in many cases their seat is not the same as that in syphilis. For example, of the bones of the skull the frontal and temporal bones are frequently affected in syphilitics, but exceedingly rarely in scrofulous subjects. Caries of the temporal bone again is of frequent occurrence in scrofula, while this bone is only rarely attacked in syphilis. The occipital plate, which is not so often affected in scrofula as in the course of lues, nevertheless becomes carious in scrofulous subjects, also when the disease extends from the vertebræ. Spondylitis, however, is a frequent accompanying symptom, especially of scrofulosis. In this disease, morever, caries of the short, spongy bones is more frequently met with than in syphilis. This preference for spongy tissue is also marked in the case of the long hollow bones, syphilis being more frequently localized on the compact diaphysis, and scrofulosis on the spongy ends of the bones. A positive diagnosis is found in the demonstration of tubercle bacilli in the pathological discharges or the presence of undoubted tuberculosis in other organs. The fact must not be overlooked, however, that scrofula and syphilis may exist together.

At all events, we should carefully examine the whole body and take into account all accompanying circumstances which speak for or against syphilis. Where positive data are absent, the success or failure of antisyphilitic treatment is considered decisive as to what the disease should be called—*i.e.*, a diagnosis is made, as we say, *ex juvantibus*. In some cases this procedure is certainly very suitable, only we must not think that every pathological product which disappears after a mercurial or iodide treatment must of necessity be syphilitic.

Syphilitic Affections of the Joints.

The same thing has happened with regard to the arthropathies occurring in the course of syphilis as in many other organic affections. Soon after this disease became generally known, and also later, syphilitic affections of the joints were mentioned by several authors. Hunter could not positively bring himself to look upon joint affections as syphilitic even when they were cured by mercurial preparations; but his commentator, Babington, very plainly distinguished acute and chronic inflammations of the joints in syphilis. Ricord, it is true, admitted the occurrence of affections of the joints in syphilitics, but regarded them as complications. Other French authors, especially Richet, defended the belief in the syphilitic nature

of this affection, and in the year 1863 Lancereaux succeeded in firmly establishing this view by anatomical research. He found well-developed gummatous formations in the subsynovial and fibrous tissue of the capsule of the knee-joint. The anatomical studies following his placed the doctrine of a syphilitic affection of the joints on a still firmer basis. From this the picture of *synovitis* and *synovitis pannosa* has been developed. There have been frequently found either circumscribed ulceration and fibrillation of the cartilage, accompanied by the formation of villous excrescences, or radiating, depressed white cicatrices in the cartilage, or finally diffused thickening of the synovia and numerous villi.

The clinical demonstration of syphilitic affections of the joints is frequently possible, and it is only surprising that they have so seldom attracted the attention of even prominent syphilologists. Observations relating to them are becoming more and more frequent in recent times.

Nearly all the joints, that of the lower jaw included, have been found affected; the knee and elbow joints are, however, most frequently attacked.

Arthralgias of the various joints are frequently observed as the first sign of a constitutional affection. They occasionally make their appearance a few days before the cutaneous eruption or contemporaneously with it and last only a short time, rarely longer than a week. I have seen inflammation of the joints during the first syphilitic eruptions or during their disappearance. Disease of the hip-joint has even been observed by me in the presence of a recent exanthem. After the administration of blue pill or injections of oleum cinereum and proper bandaging, a rapid cure was obtained. In rare cases these joint affections make their appearance under the guise of a polyarticular rheumatism, during the course of which one or another joint is suddenly affected, as shown by intense pain, and the affection becomes at last localized in one or more joints (at the same time or successively). More generally a more or less plainly marked monoarthritis or polyarthritis is present from the beginning. The patients find that the joints attacked, although freely movable within certain limits, at once begin to give pain when a full flexion or a full extension is attempted. An objective examination sometimes reveals a slight redness of the skin and increased heat, but as a rule a slight swelling or at least a disappearance of normal depressions, for example at the side of the olecranon or the patella, can be demonstrated. Occasionally a more careful palpation will also reveal one or more painful points on the extremities of the bones entering into the formation of the joint. In individual cases the joint affection is accom-

panied by high fever (generally with morning remissions) and increased painfulness. After one or two weeks involution and cure of this *synovitis*, for as such we may probably designate this process, usually obtain with a return of the normal function. Exceptionally, however, the synovitis remains stationary in a chronic, probably but slightly painful condition; or else a chronic synovitis is developed only some years after infection has taken place. These forms are accompanied by less pain and only rarely by fever. The swelling is generally greater, caused by an effusion into the joint; but the function is not greatly disturbed; in short, we are confronted by the condition of a *chronic hydrarthrosis*. The disease drags on for some time, and goes on to improvement under a proper regimen, and frequently also to a cure. Acute affections of one or more joints with a comparatively favorable issue are occasionally observed in the later stages of syphilis. As a general rule, however, the affections of the joints which make their appearance after syphilis has existed for some time are more intractable, because there will be also present, beside the symptoms enumerated (swelling, impeded movements), thickening of the capsule, which renders movement possible only with an accompanying grating and friction sound. We are here probably dealing with a *villous hyperplasia of the synovial membrane*, with or without defects of the cartilage. Pain, moreover, is not great, but the prospect of a complete cure is slight. It may even be that movements will be greatly curtailed, from a callous retraction of the thickened capsule, or ankylosis may be unavoidable.

If the swelling is confined only to individual parts of the capsule or the ligamentous apparatus, we may assume a probable *gummatous* character of the arthritis. Effusion into the joint is occasionally only slight; pain is not always intense, movement is but little hindered. The course, even when from disintegration of the gumma the joint becomes perforated externally, as I have once observed, very rarely becomes violent.

Affections of the *cartilages of the joints* themselves have also been observed, but as a rule an affection of the cartilage is accompanied by a synovial affection, or it follows in the wake of an ostitic process. When the latter occurs, gummatous foci in the epiphyses finally also destroy the cartilage in their growth towards the joint. This process is frequently met with in the phalanges; it is, however, also frequently observed in the large bones. This joint affection, which usually runs a chronic course, commonly makes its appearance only some time after infection. I have, however, observed an extension of the inflammation very early from the periosteum to the neighboring joint.

A female factory hand, 30 years of age, came to my clinic suffering with chancres on both labia and a macular syphilide. The primary sore had not yet perfectly disappeared when, in the fifth week of treatment, a painful tumor made its appearance at the lower end of the right ulna. After only a few days the pain had already extended to the margin of the joint, and the swelling also seemed now to be particularly marked at the wrist-joint, so that the latter had to be immobilized. When, after about one month, the bandage was removed, the swelling had disappeared from the ulnar side of the joint, and had extended to the radial side. The carporadial joint proved on examination to be loosened, and the cartilages—as could be surmised by the grating sound—had become denuded of their smooth surfaces. Although examination was not accompanied by especial pain, the joint was nevertheless again supported, and the bandage only removed after the lapse of eighteen more days, when the joint was found to be firm. Bathing the hand and passive motion had to be continued for many months.

We thus see that joint affections may make their appearance at any time during the course of syphilis, and that those which occur early, as a rule run a more favorable course. A distinctly unfavorable issue is, however, not to be expected even in the arthritides of the later period; although they are characterized by a slow course, and their perfect restoration to a normal condition is more infrequently observed. The thickenings and villous excrescences of the capsule are not perfectly absorbed on the one hand, and on the other are the cause of crepitation on movement of the joint, besides irregularities, defects, and cicatrices in the cartilage. The danger is, however, also great that the thickened capsule may become retracted by callosities, ankylosis resulting or at least movement being greatly restricted—a result which may also be expected after the healing of gummatous foci in the ligamentous apparatus. Obliteration of the joint by partial or complete destruction of the cartilage, the capsule, and the ligaments is generally seen in those arthropathies which originate in an ostitis or periostitis of a joint. The segments of the limb below the joint hang loose and become perfectly useless, as we may frequently observe after a phalangitis syphilitica. The termination in bony ankylosis is rare.

Diagnosis.

The diagnosis of joint syphilis is justified when other symptoms of syphilis are also found. If the joint affection only is present, its multiplicity alone would raise the suspicion of a dyscrasia, and lead to an inquiry into the antecedent history. It should furthermore be considered that a syphilitic polyarthritis will only rarely have any cardiac complications. We must also bear in mind certain peculiari-

ties of the joint affection, which are present also in the monoarticular troubles, and which consist in the fact that while intense fever and great pain may be observed in joint syphilis, on the whole the subjective disturbances will remain far behind the objective symptoms, even when large joints are involved. We should always think of syphilis, in the case of a well-nourished individual who has acquired a stubborn joint disease, even when it has been caused by a traumatism; and when due to the latter cause the trouble is the more suspicious, the slighter was the accident which it seemed to follow. The result of medication should also have some influence in judging the case. Preparations of salicylic acid have a very prompt action in acute articular rheumatism, while in syphilis of the joints an antisyphilitic treatment has a favorable influence as a rule. We should, however, remember that even an antiluetic treatment will not do any good when irreparable destruction of the joint is present.

The Muscles.

It is not improbable that some part of the rheumatic symptoms, which so frequently occur among the first signs of a constitutional syphilis, either preceding or accompanying the skin eruptions, may have their origin in a slight irritative myositis.

I have in a few cases observed a distinctly developed *myositis*, during the early period of syphilis. The patient complains of pain, which he is not always able at first to locate distinctly; as movements are as a rule restricted and painful, the pain is not infrequently assigned to the joint. When a more minute examination is made, however, we find that the bones and joints, in case they are not the seat of the disease, are not tender to pressure or on percussion, while the handling of the muscles is very painful. The tenderness is sometimes confined more to the muscular tissue, sometimes more to the tendinous portion. With this the muscle feels firm and thickened, as though contracted; as a matter of fact it is usually contracted, and the attempt to overcome this, either actively or passively, causes pain.

The affection may be most instructively demonstrated in the biceps brachii, for here it is accompanied by flexion and obstruction to the movements of the elbow-joint. In some cases weeks pass by before the affection subsides, but recovery is, according to my experience, always perfect. The most common form of syphilitic disease in the muscle is the *gumma*. We find here that a firm infiltration is formed, as a rule accompanied by pain, which is located within the contour of the muscle and follows the movements of the

latter. The gumma is generally situated in the neighborhood of a tendon, although frequently also in the belly of the muscle itself. The gumma increases only very slowly and gradually becomes softer; with this the muscle is rigid, and even in a condition of contraction. This results in different angular positions of the joints. F. Guyot saw lockjaw produced by such a contraction of the temporal and masseter muscles, and before him Boyer and Bouilly twice observed a contracture of the masseter muscle as a result of myositis syphilitica.

Under the most favorable conditions absorption results. In that case, of course, the muscular fibres involved are destroyed or replaced by connective tissue; cheesy foci only rarely remain behind. As a rule, however, the infiltration spreads to the surrounding fasciæ and subcutaneous tissue which are involved in the gummatous process; the tumor bulges out more distinctly and is less movable. In the measure that the skin in the further course of the disease becomes involved it takes on a bluish-red color, and becomes adherent to the whole tumor. After softening, when the disintegrated mass had reached the surface, a large, deep, frequently sinuous gummatous ulcer is formed, from which necrotic masses (generally belonging to the fasciæ of the muscles) slough away. The course of an ulcerating gumma of the muscle is always protracted, extending over many weeks and months. After healing has occurred, a cicatrix is formed which binds the muscle or the tendon to a larger or smaller surface of the skin, which then presents distinct distortions on motion. I have observed such adhesions of the muscle or tendon with the cicatrix of the integument, in the centre of the sternocleidomastoid and at the anterior border of the deltoid, on the quadriceps, the semitendinosus, and on the flexor digitorum below the middle of the forearm. In cases in which large masses of muscles are destroyed by ulceration, a cicatrix may form which becomes directly adherent to the periosteum. This takes place as a rule when the gummata of a muscle heal in one place and extend in another direction. If besides fasciæ, subcutaneous tissue and integument have been involved in the gumma the serpiginous process also becomes evident externally. We not infrequently find a large portion of the deltoid, pectoralis major, and trapezius destroyed in this way, the very thin cicatrix being tensely stretched over the corresponding parts of the bones of the arm, the scapula, the clavicle, and the ribs, forming a marked check to the movements of the shoulder-joint. In neglected cases nearly all the muscles of an extremity may thus become destroyed.

Besides the purely gummatous affection of the muscles, an extensive *interstitial infiltration* may occur. This form of myositis begins

with pain and swelling of the muscle, or it may present the symptoms of a slight muscular rheumatism, and gradually lead to a connective-tissue degeneration of the muscle. Anatomically it may be shown that the blood-vessels of the perimysium are surrounded by granulation cells. The vessels themselves are enlarged and tortuous. A proliferation of the perimysium is also noticed. The nuclei of the sarcolemma stand close together, in a series of groups of five to twelve resting against each other. The contractile substance is not at first essentially changed in its structure. Later on the interstitial connective tissue becomes more and more filled with cells, the muscular fibres become narrower, and after the process has run its course, they are wholly replaced by connective tissue. Occasionally different kinds of degeneration may be observed in the muscular fibres themselves. As a rule this form is combined with the gummatous myositis in such a manner that gummata of the muscles alternate with the interstitial infiltration, or that small gummatous foci are mixed with the latter (callous gummata of the muscles). The muscle then becomes uneven in places and shortened, while at other points gummata which are ready to burst frequently undergo a long-continued suppuration on account of their rigid surroundings. After this form of myositis no such extensive loss of substance and cicatrices are left behind as after the gummatous form, but instead the destruction of the contractile substance is much more extensive. Thus I have seen in a female patient a loss of muscular movement of the soft palate and could not induce contractions by electricity in a large portion of the sternocleidomastoid muscle.

That a syphilitic *myositis ossificans* may occur in rare cases has been mentioned already.

In the course of syphilis *atrophies* of single muscles, for example the triceps and the flexor muscles of the forearm, or of whole muscle groups of the upper or lower extremity have been observed. These do not seem to represent an individual muscular affection, but rather are dependent on a syphilitic affection of the nerves. F. Dejerine has demonstrated this anatomically in a case which presented atrophy of the general muscular system of the lower extremities and paraplegia, as a result of syphilis.

Distinctly marked affections of the muscles will only rarely be observed in the first stage of a syphilitic infection; most likely only in grave early forms of lues. As a general rule syphilis of the muscles is observed after the disease has existed for some time. We shall, therefore, frequently meet the affection under discussion in connection with signs of recent or past syphilitic processes in other regions.

The affection generally makes its appearance in several parts of the same muscle, more frequently still in different muscles at the same time. Thus I found in one of the above-mentioned patients, suffering with extensive muscular disturbances, a concomitant affection of the left scalenus anticus and total loss of the clavicular head of the right sternocleidomastoid; and in another female patient I found the right sternocleidomastoid, the buccinator, the masseter, and the muscles of the soft palate converted into connective tissue. In still another case, also in a woman, the frontal, zygomatic, masseter, deltoid, triceps, supinator longus, ulnaris externus, gastrocnemius, and tibialis anticus were in part invaded by recent gummata, in part destroyed and replaced by cicatrices.

Diagnosis.

If only a single muscular gumma of large size is present, it may be mistaken, if other syphilitic symptoms are overlooked or if they are absent, for a neoplasm. Doubts which arise in a case of this kind will be most rapidly cleared up by the tentative institution of an antisyphilitic treatment. Nevertheless we find cases reported up to recent times in which gummata were mistaken for sarcomata or for some other neoplasms and were extirpated. An anatomical examination even does not always give us the desired information. On the other hand, we may also be led to mistake multiple disease foci in the muscles for gummata. In this relation a case reported by R. Koehler is remarkable. A woman, forty-four years of age, presented, in addition to cicatrices on the soft palate and the right lower limb and ulcers on the malleoli and other parts of the integument, a whole series of large tumors in the muscles. These were taken for gummatous nodules until, after repeated examinations, it was discovered that the pus from a gluteal tumor contained *actinomyces*. Enlargement of the spleen occurred and was accompanied with pain in the hypochondrium. The patient went into collapse and died with remittent and at times very high fever. At the autopsy O. Israel found the ray fungus in the spleen, heart, and lungs, and cicatrices in the liver.

The Tendons.

Distinctly marked swelling of the sheaths of the tendons has been described by Hermann Hoelder. On the tendon sheaths of the fingers Verneuil observed acute, only slightly painful hygromata occurring in the early stage of syphilis; the skin remained normal. A cure was easily effected. Alfred Fournier is said to have seen similar

hygromata in nearly all the tendon sheaths, and he distinguishes, in addition to the hydropsies, a synovitis of moderate degree, which is sometimes spontaneously painful, but always so on voluntary motion. I have observed a gummatous cavity the size of a walnut, on the base of which the diseased tendon of the flexor digitorum communis was lying bare. The patient was a young girl who had acquired syphilis only a short time before.

The Bursæ.

Affections of the bursæ have also been observed in the course of syphilis. In a patient at my clinic, a woman fifty-six years of age, suffering with an initial lesion and roseola, a hygroma of the bursa mucosa semimembranosa dextra made its appearance in the form of a distinctly defined fluctuating and moderately tender tumor larger than a thumb; after a course of treatment lasting four months hardly a vestige of it was left. Subsequent to that I frequently saw a similar bursitis semitendinosa* in an early period of syphilis, and at one time a bilateral bursitis of the olecranon; here also a rapid cure was obtained with antiluetic treatment. Fournier mentions a hygroma of the bursa præpatellaris, Verneuil a painless fluctuating tumor of the bursa olecrani in a man who had at the time a roseola. The same author also mentions affections of the bursæ in other regions. Couteaud observed a hygroma of the bursa mucosa of the ileopsoas, six years after infection, which was cured by antiluetic treatment.

A gummatous bursitis trochanterica was twice observed by me. In one case a tumor larger than a biscuit was situated under the skin corresponding to the bursa of the left trochanter, in which solid points alternated with fluctuating ones. On walking as well as on examination only moderate tenderness was present. From two distal openings there exuded a large quantity of turbid, sticky fluid, mixed with solid particles. After the cavity had been drained and iodoform emulsion poured into it, constitutional treatment being also instituted, it soon closed and the other symptoms of lues also disappeared. In the other patient the bursitis also made its appearance on the left trochanter, following a traumatism. On account of great suffering the cavity was opened and cleaned out (being filled with rice-like bodies). In spite of surgical treatment, continued for a long time, the disease was not arrested until an infiltration which made its appearance in the neighborhood led to a suspicion of lues, which was corroborated by the patient's confession of having been infected

* The sartorius, semitendinosus, and semimembranosus are inserted in the median condyle of the tibia, so near together that the clinician can only with difficulty decide which of the respective bursæ is diseased.

a year previously. Iodide of potassium and decoctum sarsaparillæ inspissatum, together with the local application of iodoform emulsion, finally brought about a cure.

E. L. Keyes has observed a gummatous degeneration of the bursa præpatellaris in five cases. The bursal tumor was occasionally hard as a board to the touch, occasionally it was fluctuating; it developed slowly and without pain. When left to itself, fistulæ or ulcers were formed.

The Fasciæ.

I have seen infiltrations of the fasciæ in the form of hard, only slightly tender nodules, in the early period of syphilis. These may also be found independently in the ligamenta intermuscularia. I have in one case seen a gumma the size of a fist in the ligamentum intermusculare externum of the arm, which had involved neither the biceps nor the triceps. As a rule, however, such gummata involve the neighboring tissues.

SYPHILIS OF THE NERVOUS SYSTEM.

Soon after syphilis became known it was observed that the internal organs, including the nervous system, might also become affected by the disease. Later the idea arose that the affections relating to the nervous system were caused by syphilitic disease of neighboring bones, namely, by caries or necrosis, tophi, or gummata (Fallopius, Botal). The gummatous process affecting the brain was, however, also recognized. Hunter, to whom our thanks are due, it is true, for other great discoveries in medicine, caused a step backward by teaching that he had never observed syphilitic affections of the internal organs nor of the brain. As, however, affections within the nervous sphere could not be denied as occurring in the course of syphilis, and also as depending on it, the old idea of Fallopius and Botal was taken up again, and such cases were explained by the assumption that syphilitic deposits on the bones of the skull were the cause of an existing disturbance of the brain.

It was not until the second half of the present century that the study of cerebral syphilis was taken up again, and the reports of such cases were received more seriously. The works then and later published rendered the conviction more and more fixed that cerebral symptoms are only rarely due to exostoses.

We must not, however, go to the other extreme and think that cerebral symptoms are never produced by bone syphilis. We have previously reported a number of observations bearing upon this point.

Another circumstance, however, has also been an obstruction to the study of cerebral syphilis. As we have seen, Ricord had laid down a formal progression in the affections of the various tissues and organs, which found a rigid expression in his "secondary" and "tertiary" syphilis. According to this classification disturbances of the nervous system were relegated to the "tertiary" period and thus a Procrustean bed was made which rendered any unprejudiced observation impossible. Virchow antagonized Ricord's idea most effectively and most successfully, by opposing anatomical facts to hypotheses, and in his work "Natur der constitutionell-syphilitischen Affectionen," established the rule that the processes which make their appearance during the course of syphilis, present themselves in part as simply irritative (inflammatory and hyperplastic), in part as specific (gummatous) affections, and that every organ may become affected during the course of syphilis in the form of a simple hyperplasia or of mere irritation, as well as in a gummatous form; that, therefore, the irritative changes, which are more often met in the early period of the disease, may also occur in the visceral portions of the body, which according to Ricord become affected only in the "tertiary" stage. This teaching of Virchow opened the way freely to unbiassed observation in the field of syphilis, and at once instances of the affection of internal organs, especially of the nervous system, in all the stages of syphilis began to increase in number.

To all appearances the nervous system, of all internal organs, is most frequently attacked by syphilis. The frequency of nerve syphilis, which has been recognized only in our own day, is considerably increased, if we also admit the many cases of progressive paralysis and tabes, which of necessity must be looked upon as dependent on syphilis (see below). According to my experience we must also take cognizance of the irritative changes dependent on syphilis, which occur in the central nervous system.

I have repeatedly observed that patients in the first stage of syphilis occasionally suffer with *headache*, *vertigo*, and a sort of *irritability;* some of these also looked very ill, and they complained of *nausea;* the temperature rarely rose more than a few tenths of a degree Centigrade, and the pulse rate was seldom accelerated. These conditions, it is true, lasted only a few days, but they appeared in such an accentuated form that it seemed perfectly justifiable to ascribe them to hyperæmic or perhaps even to slight infiltrative changes in the meninges, and perhaps also in the brain.

We shall study these symptoms later under the designation "meningeal irritation," which is also looked upon by Franz von Rinecker as the only proper one and which has been adopted by other authors.

We may also point out that although the meningeal irritation sometimes accompanies the syphilitic eruptive fever, the meningeal conditions of irritation also frequently persist after the skin eruption, or else they manifest themselves a few days after the syphilide has appeared or at a time when the syphilide is already beginning to disappear. These meningeal irritations, according to my present experience, present some analogy with the irritative condition of the skin in syphilis in so far as here also restitutio ad integrum is the rule.

Conditions of this kind have been already pointed out more than once by various authorities. Thus Sigmund has demonstrated that during the "secondary" period among other symptoms we often find rapid emaciation, digestive disturbances of various kinds, pain in different parts of the body, most frequently in the head and neck, in the joints, the muscles, etc., disturbance of sleep, lassitude, and mental irritability. Kussmaul expresses himself in like manner. Lancereaux mentions the occurrence of neuralgias during the course of the "secondary period," "avec une céphalie opiniâtre"—which rapidly improved under iodide of potassium, and on which quinine had no effect.

Alrik Ljunggrén takes directly for granted the "undoubted but only temporary occurrence, during the first stage, of hyperæmia of the cerebral meninges or of the interstitial matter," as "from a clinical standpoint various conditions speak for their true existence"; and he compares them to the simple hyperæmic forms of skin affections. My attention was first attracted to conditions of meningeal irritation in the early stage of syphilis in the year 1878. Later observations have more and more strengthened my conclusions that these meningeal irritations in the first stage of syphilis should not be counted as rare. In these meningeal irritations pain is either distributed over the whole skull, or it occupies only the forehead or the occiput. Occasionally there is a painful band extending vertically over the head from one ear to the other; or the patient describes the sensation as one similar to a constriction of the head in a horizontal line; or the pain is experienced only in the posterior part of the skull, reaching from one ear to the other; occasionally the pain makes its appearance as an occipital neuralgia. Besides this the patients complain of vertigo, rarely nausea, anorexia, and ill humor and mental irritability. Objectively, moreover, an *irregularity in the size of the pupils* (very likely due to a paralysis of the sphincters) or a marked *slowing of the pulse* can be demonstrated. These conditions, however, usually last only a short time and are very soon followed (especially after a few doses of mercury) by the previous well-

being; only in one or the other case will the symptoms of irritation present a stubborn character. Occasionally a neuralgia of the dura mater may be added.

The probability of my supposition that in individual cases the meningeal irritation may be increased to an infiltration, bordered on the positive, when my supposition that similar irritative changes in the early stage of syphilis might be especially demonstrable in the fundus of the eye, was in the course of events fully corroborated. Professor Isidor Schnabel, at my request, examined ophthalmoscopically patients in the early stage of syphilis, and out of forty found the fundus of the eye of a normal color in only nineteen; in fourteen of the remaining twenty-one he was able to demonstrate choroidal irritation of different degrees, and in seven he found inflammatory processes of the choroid or retina or of both membranes. These changes in the fundus of the eye, which were repeatedly present in the early stage of the general syphilitic affection, frequently attained such a high degree as we find otherwise only in retinitis with total abolition of the visual function, and still the visual disturbances were either altogether absent or were only of a subordinate character.

I believe, therefore, that I am justified in a totally analogous manner in assuming the presence of marked infiltration in the meningeal irritations designated by me as syphilitic affections, which besides also frequently present a high degree of retinal irritation that cannot be distinguished from retinitis, although clinically only the slight disturbances already mentioned can be found.

How slightly marked may be the symptoms even of a syphilitic meningeal irritation which is accompanied by infiltration can best be seen from a case of syphilitic meningitis reported by Griesinger, which made its appearance six months after infection in a baker thirty-eight years of age, and finally ended in death. For four weeks "a quiet and somewhat stupid manner was observed in the patient, which was not considered morbid, however, but natural to the individual. He had also complained, now and then, besides being pale, of pain in the temples, vertigo, disturbed sleep, which in the first instance could be credited to the mercurial treatment." All these symptoms would undoubtedly have remained unobserved if the process going on in the cerebral meninges had retrograded. The slight symptoms, however, at once gained importance when the cerebral symptoms, in their further course, became more and more marked and graver.

As we shall see later on, the clinical symptoms point also to the supposition of a like irritation of the spinal meninges.

In the course of the syphilitic process a pronounced meningitis

and inflammation or softening of the brain are also observed. We must here emphasize, however, the fact that a pure meningeal inflammation as a rule occurs in cases which arise from the extension of a suppurative process of the bones of the skull—a syphilitic caries or necrosis (see above). Aside from this there is, however, also an independent inflammation of the cerebral meninges, which is not due to a gummatous meningitis ending in connective-tissue callosities. *Pachymeningitic* affections are certainly frequently met with; at least one is often enough led to the assumption, by the presence of a constant pain in the head, which is sometimes increased by percussion of the spot, without the possibility of demonstrating any other changes *in loco* or any side disturbances. Obviously we are dealing here with quasi circumscribed periosteal processes on the inner surface of the skull. *Pachymeningitis hæmorrhagica* accompanied by the formation of *hæmatoma* has only rarely been observed. We shall refer to a notable case of this kind later on.

Ependymitis with a collection of fluid in the ventricles (*hydrocephalus internus*) has been diagnosed by W. F. Laschkiewitz in three syphilitic subjects, and in two cases the diagnosis was confirmed at the autopsy.

Pure encephalitides seem to occur but rarely in the course of syphilis. The *foci of softening*, which were formerly looked upon as encephalitic, are probably only the final result of the affection of the arteries described above.

The *endarteritis* spoken of in that part, which is so readily developed during the course of the syphilitic process, will of necessity deprive individual portions of the brain of their nutrition and injure their functions. If, in addition to the endarteritis, the artery has been totally obliterated by the changes described or by the addition of thrombi, a softening of the regions of the brain supplied by it can be looked upon merely as a natural consequence. According to Heubner's researches the carotids and their branches, the arteriæ fossæ Sylvii and corporis callosi, are most frequently attacked in their first portions by the endarteritis. From these first portions, however, are derived the terminal arteries of the lenticular nucleus and the caudate nucleus, in which parts foci of softening are most frequently met with.

Fr. Chvostek has observed encephalomalacia as a result of syphilitic endarteritis in two cases, in two chronic inflammation and consecutive atrophy of the cortex of the anterior lobes, and in two cerebral hemorrhage.

While formerly *hemorrhages* of the brain were looked upon as rare, we now know that these are of frequent occurrence. From the

results of the anatomical researches at our disposal, we are led to refer the hemorrhages to the formation of aneurysms in the diseased vessels (Th. Rumpf, Paul Spillmann, Thibièrge, and others), which aneurysms are quite frequently observed in syphilitic subjects (see above).

Gummatous products are fairly often found in the membranes of the brain. In the dura mater the gumma is developed between its layers, and with especial predilection in their duplications (falx, etc.). The neoplasm is spread over a large extent of surface or occurs in the form of circumscribed tumors. The gummata of the dura frequently reach the size of a walnut and over, and consist most frequently of dense fibrillary portions studded with cells, which frequently carry with them the signs of a fatty degeneration. While other changes are not met with within the skull in the gummatous affection of the dura, the roof of the skull corresponding to the gumma seems to be occasionally eroded. The case is different with the circumscribed gumma of the pia mater. This generally leads on one side to an adhesion with the dura, on the other to a union with the contiguous surface of the brain. It very frequently presents the aspect of a reddish jelly-like tissue rich in cells, and in the neighborhood only a few small, dry gummatous formations are to be seen. The gummata which most frequently appear on the upper and lateral portions in the majority of cases pass not only to the contiguous cortex, but also to the white substance. When this is the case, softening of the surrounding brain is not infrequently absent. At the base of the brain the dura mater as a rule is not involved in gummata of the pia. The meningeal gumma, however, also appears in the form of a diffuse jelly-like infiltration, which may present the character of a past meningitis in its origin as well as also in its further course by a transformation of the jelly-like product into a connective-tissue-like cicatricial membrane.

Meningitis gummosa basilaris diffusa is very frequently encountered; it is, indeed, the most frequently observed luetic affection of the brain. The neighborhood of the chiasm is generally the point of origin of the process in which the oculomotor, optic, and other cerebral nerves are not infrequently included. Less frequently the diffuse gummatous meningitis will be observed on the convexity. Common as it is for the gummatous affection of the pia mater to lead to gummatous formations in the contiguous brain surface, it is in like measure rare, according to Heubner's tabulation, for gummata to occur within the brain independently of any growths on the surface. Heubner believes that in such cases the gummata of the cortex gradually extend into the interior. A few gummata have, however, been found

within the brain. But in whatever part the gumma may be found, some of the neighboring arteries will present the obliterating affection above described, the result of which will be softening of the brain around the gumma.

Besides the anatomical changes described above, syphilis undoubtedly also causes other serious alterations of the central nervous system, although we are at present unable to trace their relation to lues. We are speaking here of processes which present in their final stage *degenerations*, and are the cause of many important forms of disease, among which we may mention ophthalmoplegia, immobility of the pupils, atrophy of the optic nerve, dementia paralytica, and tabes.

The Brain and Its Meninges.

Syphilitic affections of the brain and its membranes, so far as elements which preside over the most important functions of life are involved in the disease, will lead to the same symptoms as other morbid changes within the cranial cavity. Increased irritability within the motor, sensory, or mental sphere, paralysis in these areas, lowering of the intelligence and power of thought, psychoses of the greatest variety are produced by syphilis as well as by other processes. And still in taking a general view of the symptoms, certain differences are found in many cases, which call for an individual symptomatology. But this frequently fails us, and we find it necessary, therefore, in finally arriving at a diagnosis, not only to inquire carefully into the history of the patient, but also to study the further course of the disease, as well as the result of treatment.

A very constant symptom in this affection is headache. It attacks in an intense form either the whole head or only a part of it, and may increase at certain times of the day, but only rarely presents total intermissions. We cannot deny that the headache in many cases shows great exacerbations, particularly at night, but it is altogether wrong to speak of the nocturnal character of the headaches of syphilitic origin as peculiarly distinctive. If the headache is merely a result of the meningeal irritation, mentioned above, it only exceptionally continues longer than one or two weeks, although it may last several weeks in cases not treated. When the headache recurs at intervals of weeks or months, the seat of the intense pain as a rule also changes at one time or another. The longer the headache continues, the more certainly may we also expect other grave symptoms on the part of the central nervous system. Long-continued pain confined to certain portions of the head may frequently be referred to a neuralgia of some nerve branch of the dura, and may sometimes be

made use of as a basis for a topical diagnosis. Quite frequently the headache is accompanied by vomiting.

At times neuralgic pains are very marked, and the patients complain of insomnia, mental irritability, a flickering before the eyes, and various other paræsthesiæ. Less frequent are attacks of vertigo which occasionally appear spontaneously, but which may also be brought on by mental exertion.

When the cephalic symptoms are of longer duration there is added a certain obstruction to the power of thinking, and loss of memory. Together with this attacks of unconsciousness combined with convulsions may occur.

Changes in the pulse rate, especially a retardation, are also observed; at other times the pulse is accelerated or irregular.

Polyuria and polydipsia, as symptoms of a cerebral affection, have frequently been observed in syphilis of the brain.

Optic neuritis or choked disc is also frequently found in diseases of the brain and its membranes; with this the visual power either remains normal or is disturbed in a variety of ways. An optic neuritis running a chronic course, according to W. R. Gowers, is an argument against the diagnosis of a syphilitic tumor of the brain.

Quite frequently the diagnosis of cerebral syphilis must be made from these general symptoms alone. In *hydrocephalus internus syphiliticus*, *ependymitis syphilitica*, violent headache, as so frequently happens in cerebral syphilis, is most prominent. This does not occur periodically, but is continuous and occasionally subject to excessive exacerbations. It is accompanied by nausea and vomiting which is brought on with particular ease by movements of the head or change of position. Neither convulsions nor paralyses are present. The pupils, which are generally dilated, react well to light; the visual power is diminished; the fundus of the eye is passively congested; the psychic functions are in time weakened (Laschkiewitch).

When parts are attacked, disease of which leads to disturbed functions, we get certain functional or focal symptoms which permit of a topical diagnosis. Physiological and pathological researches of a few decades past have led to very important results in that direction, in so far as in many cases certain irritative focal symptoms permit us to arrive at positive conclusions as to the seat of the disease in the brain.

According to these researches the motor tracts take their origin from the central convolutions and pass, while gradually becoming narrower, through the corona radiata, internal capsule, cerebral peduncles, and pons to the crossing of the pyramids. From this course it is clear that a focus of a certain size in the cortex will cause only a cir-

cumscribed paralysis, a monoplegia, while one of equal size, situated say in the internal capsule, where the fibres coming from the cortex are crowded together in a small space, may produce a complete hemiplegia. As a matter of fact, then, monoplegia is a prominent symptom of affections of the cortex. Such monoplegias, isolated forms of paralysis, are frequently met with in the leg, the arm, and the face. Still more frequently monoplegia facialis and brachialis occur together, while monoplegia cruralis and brachialis are much less commonly associated.

A paralysis, however, can be referred with certainty to a lesion of the cortex only when symptoms of irritation—convulsions—are present in the previous paralyzed parts.

According to Nothnagel partial jactitations, confined to single muscular areas, which make their appearance at the beginning of a cerebral hemorrhage or softening, or when a tumor is developing, and which are followed by a paralysis of the affected muscular area, permit one to assume with great probability, but not with certainty, the existence of a cortical focus. A cortical lesion may, however, with certainty be assumed, if the partly clonic contractions appear only at a later period in the previously paralyzed parts. M. Jastrowitz expresses himself even more positively in this sense. The convulsions may also affect isolated regions or may occur in many parts (arms and face); they may even involve an entire half of the body—cortical epilepsy, Jacksonian epilepsy.

The motor cortical area is situated in the anterior and posterior central convolutions and in the (medianly situated) lobulus paracentralis; furthermore in the contiguous portion of the superior parietal lobe, perhaps also in the gyrus frontalis superior.

In general, the upper portion of the central convolutions, especially the lobulus paracentralis, is the centre for movements of the leg; the middle portions (anterior) of the central convolutions control the arm; those below innervate the face and tongue. The tactile cortical areas act, according to S. Exner, as a rule, with the motor areas, and C. Wernicke is fully in accord with Munk when he calls the so-called motor region the tactile region. On the other hand, according to Nothnagel's researches, the localities of the surface of the brain lesions of which cause on the one hand motor paralysis, on the other disturbance of the muscular sensation, although situated near together, are not identical. The observations of Th. Rumpf in this direction possess great interest. He reported two cases of syphilitic disease of the cortex in which, except for a monoplegia, there was not the slightest disturbance of sensation in the parts corresponding to the central lesion, and the sensation of the skin also remained

intact. From this Rumpf concludes that the so-called motor centre and that of sensation are not identical. In two other patients again he found monoplegias with convulsive attacks, but in these the sensation of the involved extremity was defective at the same time that the motor power was. In these cases he thought himself justified in assuming a syphilitic cortical affection in the tactile sphere.

Numerous clinical and pathologico-anatomical experiences teach us that these centres are indeed very frequently the seat of syphilitic affections, that even a cortical epilepsy is more frequently grounded in syphilis than in any other cause. Lancereaux and Fournier noted the occurrence of convulsions in single members, and Charcot minutely described cases of this sort. This phenomenon is, however, usually ushered in by *monoplegia* or *hemiplegia*, and only later convulsions appear, which sometimes end in true epilepsy. With this consciousness may sometimes be abolished, but it is also often found but little disturbed. As a rule the partial or hemiplegic form is more often found. The attacks are preceded generally by an increase of the headache, which is already present in unilateral character, or which radiates from a single point to the face and throat. Now one extremity is attacked by tremor or a rhythmic muscular contraction, which extends to the other extremity of the same side, and finally involves the muscles of the face and head. The mind is obscured during the extension of these jactitations, and the patient falls down, if this has not already been caused by the convulsive jactitation of one lower extremity. An attack of this kind may last an hour or longer. Frequently some obstruction of speech, sluggishness of memory, or some other abnormal symptom, such as a weakening of the extremity involved, is left behind for a shorter or longer period. Then a period of relative well-being follows, and after weeks or months there will be another attack of the same kind or differing from it. Occasionally these attacks recur daily, and always at the same time.

As is generally the case in partial epilepsy (Bravais, H. Jackson), so also in that dependent on syphilis according to J. M. Charcot, a certain rule is observed in the order of jactitations, which generally have a tendency to extend. If the convulsions begin in an upper extremity, the lower extremity will be attacked by jactitations only after the face; if the face is attacked, the convulsive movements spread first to the upper and then to the lower extremities; finally, convulsions which begin in a lower extremity, advance first to the upper, and then to the corresponding half of the face. The convulsions never occur in the order: leg, face, arm, or arm, leg, face. In partial epilepsy, clouding of consciousness as a rule begins only when the convulsions attack the face.

I once observed an exquisite case of cortical irritation in a man over 30 years of age. The left upper extremity presented spastic contractions, which were particularly strongly pronounced in the digital flexors. The more the attention was directed to this phenomenon the less could the spasms be controlled; they diminished if the arm was thrown over the back, and ceased wholly during sleep. The muscular system was here strongly developed, more so even than on the right side. The patient showed great strength in the left hand and was able to carry heavy weights with it. Sensibility was intact. The patellar reflexes were somewhat increased, otherwise the lower extremities seemed to be in a normal condition, and no paralytic symptoms could be discovered in the region of the facialis or elsewhere. In the region of the coronary suture on the right side a marked flat enlargement of the frontal bone was present; but it was not tender either to pressure or to percussion. This man had been infected seven years before and had had the symptoms of constitutional lues. One year after infection recurring eruptions made their appearance accompanied by headaches, which were especially severe on the right side. These lasted two or three years, until the patient woke up one morning with paralyzed left extremities, although retaining full consciousness. In the course of a few months the left leg recovered, while the left arm, which was insensible to the prick of a needle for only a few days, remained paralyzed eight months longer. Then spasmodic contractions occurred in the left arm, and never again ceased. There were no disturbances in defecation or urination. Until quite recently, beer and wine could be taken only in minimal quantities, and occasionally vertigo and numbness of the head were experienced in the morning. During this whole time, mercury and the iodides and later electricity were employed, without, however, changing the condition in any way. The headaches, which lasted for years and which were located chiefly on the right side, were obviously due to a pachymeningitic process of this side, which had in the course of time in all probability led to connective-tissue deposits. Into this there may have been a sudden hemorrhage which caused a left-sided hemiplegia. The newly formed deposit, especially, however, the extravasation into it, certainly did not correspond to the thickening which was felt externally, but they had their seat, without any doubt, behind the coronary suture, in the neighborhood of the central convolutions of the right side; for only in this manner could the appearance of the hemiplegia on the left side be explained. The disappearance of the paralysis and the occurrence of permanent convulsive movements in the left upper extremity, without any other psychic disturbance, point to the fact that absorption of the extravasation (and of the neoplasm) occurred towards the median line, while the pachymenigitic deposit became ossified externally and exerted a continuous pressure on the central convolutions of the arm centre.

In only a few cases have disturbances of sensation been noted.

When consciousness is retained the convulsive form of the disease may occasionally simulate *chorea*.

In a case observed by Ewald the picture of a hemiathetosis was

present, in all probability produced by a cortical affection based on lues. These clinical observations are also corroborated by anatomical findings. Thus W. Gujkiewicz mentions a case of Jacksonian epilepsy of the left side in which pain was experienced in the right temporal region, especially when the skull was percussed. Ten years previously, and again a few months before, an injury was received on the right frontal and temporal region; there was no suspicion of lues present. When antisyphilitic remedies gave only slight relief and the intensity of the symptoms increased, the patient was trephined. A tumor was discovered in the neighborhood of the right motor centre, histological examination of which justified a diagnosis of lues cerebri. After the operation improvement occurred and a cure was obtained under antiluetic treatment.

Leloir found in a syphilitic man, who during life had a paralysis of the right arm with cyanosis and who died later of tuberculosis, besides miliary tubercles in the anterior central convolution, adhesions and thickening of the membranes of the brain. This thickening, which involved the whole of the gray substance and a strip one millimetre broad of the white, and which was of a reddish to grayish yellow color, was looked upon by Leloir as a gummatous process. H. Oppenheim observed at autopsy a hyperostosis of the left cranial vault, and a diffuse gummatous meningitis arising from the dura, in the vicinity of the left frontal lobe, the central convolutions, and the neighboring portions of the left parietal lobe. The patient was a man thirty-nine years old. During life there had been tenderness to percussion of the left side of the skull, paresis of the right extremities, disturbance of the sense of position in the right foot, clonic jactitations, and paræsthesiæ, which extended from the right foot to the right half of the body; and after an attack, aphasia and hemiparesis dextra.

It should, however, be mentioned that these symptoms may also occur without any disease of the central convolutions. Thus Byrom Bramwell has described cases of epileptic attacks occurring without any disturbance of consciousness, and one of hemiplegia of the left side in which there had been a wonderful improvement under large doses of iodide of potassium and small doses of mercury. When the patient, who had been infected seven years previously and was thirty-four years of age, died later on after a convulsion lasting three days, the dura was found adherent to the brain in the posterior portion of the second right cerebral convolution. On section the posterior portion of the middle and upper frontal convolutions was found to be replaced throughout its whole extent by a firm gumma. The central convolutions and the rest of the brain were in a normal condition.

In cases of Jacksonian epilepsy occurring without corresponding

lesions in the cortex, we may remember that, though it is usually caused by solitary gummata and diffuse gummatous processes, which especially attack the anterior central convolution, or by cicatrices in these regions, similar attacks may also be excited by the products of syphilis in another location. Thus during treatment they seem to be aroused occasionally, as it were, by an irritation due to absorption of the morbid products from other parts (Paul Rowalewsky).

We have several times mentioned aphasic conditions. As we know, the speech centre is found, in right-handed persons, in the left lower (third) frontal convolution (Broca's convolution) and in the first temporal convolution.

In one case I observed, about ten years after infection, during which time repeated syphilitic symptoms (papules, iridochoroiditis, neuralgias) had been noted, the sudden occurrence of a *motor aphasia*, which gradually improved again. The patient, as I find from later reports, succumbed to grave cerebral disturbances. C. Wunderlich mentions the case of a man in whom cerebral syphilis ended in incurable idiocy, the first symptom of which was a sudden loss of speech. This attack was soon recovered from, but other similar ones recurred from time to time until a grave disturbance of speech became permanent. In one of C. Wernicke's cases, a sudden aphasia accompanied by agraphia and alexia, together with a paralysis of the right arm and of the face, made its appearance, after a previous paresis of the left arm.

Among the most important accompaniments of aphasia are alexia (inability to read, though vision is intact) and agraphia (inability to write, though motility is undisturbed). Occasionally alexia alone is present. In a man, about thirty years of age, who had acquired lues only a few months previously and was suffering from an ulcerating syphilide, I observed alexia without any other symptom on the part of the brain or the eye. Under antisyphilitic treatment the alexia disappeared together with the cutaneous symptoms. This disturbance is usually caused by an affection of the left gyrus angularis.

The temporal lobe seems to contain the centre for both auditory nerves; at least it has been observed that the disturbances of hearing of the crossed side begin to improve, in affections of this lobe, after treatment is begun. Disturbances on the part of the eye in the course of cerebral syphilis are frequently observed. We shall first consider those based on a cortical affection. The result of much research has taught us to recognize in the occipital lobe the cortical centre of the visual organ, and moreover the right half of the visual field of both eyes corresponds to the left occipital lobe, and vice versa; so that in

affections of the visual centre on one side a homonymous loss of the opposite half of the visual field of both sides occurs (hemianopsia).

With great frequency, perhaps indeed most frequently, the *base of the brain* is subject to syphilitic affections. The syphilitic neoplasms, in the form of *diffuse* or *circumscribed gummatous* infiltrations, frequently take their origin here also from the meninges. As the cerebral cortex is involved in meningeal affections at the convexity of the brain, so the cerebral nerves will be involved in affections at the base, but with them also the neighboring portions of the brain. The symptomatology is therefore composed of disturbances which on the one hand correspond to the involved cerebral nerves, on the other to the involved cerebral areas. Besides, very characteristic endarteritic changes of the cerebral arteries nearly always accompany a basilar meningitis, whereby various lesions (hemorrhages, softening) are occasioned.

Syphilitic basilar meningitis, however, is also frequently complicated by spinal lues. We can, therefore, imagine that the symptomatology under these conditions is subject to manifold modifications.

We should, however, not overlook the fact that every symptom which may point to a local disease of the brain may be absent occasionally, even in cases of extensive destruction. Thus Rumpf mentions the case of a gumma at the base of the brain, the size of a hen's egg, which had flattened the frontal lobe in its middle portion, and had given rise only to headache, terminating in coma, during life, but no symptoms of paralysis or of irritation. The right olfactory nerve had been flattened by the tumor, and transformed into a mass of connective tissue.

As regards the cerebral nerves, the affection sometimes confines itself to single nerves or their branches. In consequence, however, of the great area which luetic basilar meningitis usually occupies, we frequently find quite a number of cerebral nerves involved in the process. Optic neuritis, choked disc, and finally atrophy are quite often met with. Not infrequently the affection extends forwards to the olfactory and optic nerves, backwards to the trochlears, trigeminus, and abducens, and further to the facial and auditory nerves; or the gummatous infiltration becomes localized in the posterior meningeal portions and attacks the hypoglossus, vagus, etc.

As a general rule the neighborhood of the chiasm is affected in basilar meningitis, and this explains the frequent involvement of the nerves of the ocular muscles which pass in that direction.

As a characteristic symptom of syphilitic affections of the base, H. Oppenheim mentions oscillating hemianopsia bitemporalis. According to Oppenheim's view we are dealing here with a tissue that

is disposed to swell on account of its wealth of vessels, and in this case the appearance and disappearance of the hemianopsia would have to be referred to the presence and absence of swelling in these parts. If the basilar meningitis attacks mainly the posterior portions, we shall rarely fail to note symptoms referable to affections of the pedunculi cerebri, the pons, the cerebellum, or the medulla oblongata, according to the localization of the lesion in each special case.

According to Nothnagel the crossed forms of paralysis are characteristic of affections of the cerebral peduncles, in which the cerebral nerves, especially the oculomotor, of the side corresponding to the location of the lesion, and the extremities of the other side are involved—"hemiplegia alternans superior" (E. Leyden). Basal processes, it is true, may cause similar symptoms, and these are present with especial frequency in syphilitic basilar meningitis. However, according to Nothnagel, the alternating paralysis will point with certainty to a lesion in the pedunculus cerebri, if it makes its appearance at the same time.

If the crossed hemiplegia affects together with the extremities of the one side the facialis of the other, we have the symptom complex called "hemiplegia alternans inferior" (Gubler). The paralysis of the cerebral nerves, as might be expected, appears on the same side as the affection of the peduncles, while the body is affected on the opposite side, as the crossing of the motor fibres passing from the cerebral cortex to the spinal cord takes place lower down in the pyramids.

Affections of the *pons* are manifested according to their extent and complications in various forms. It is noteworthy that in affections of the pons the facial seems more frequently implicated than in affections of the pedunculi; in addition we find recorded in most cases also disturbances of speech and of deglutition.

Not very infrequently in cases of syphilitic arteritis the picture of an acute bulbar paralysis is caused by softening of the pons. Involvement of the region of the corpora quadrigemina as a rule causes a bilateral lesion of the branches of the oculomotor as well as disturbances of equilibrium and of coördination, as in lesions of the cerebellum (Nothnagel).

Affections of the *cerebellum* are characterized, as has been positively determined by clinical observations and experiments on animals, by a peculiar change in the gait and by disturbances of equilibrium. The patients walk with a straddle and with an unsteady gait like that of a drunken person. The reports on syphilitic affections of the cerebellum are, however, only few in number.

Affections of the *medulla oblongata* are dangerous, as nerve centres

important to life are here present. Most frequently foci of softening are found in the medulla oblongata. Fr. Mosler observed softening of the left half of the medulla in a man who at first suffered only from polyuria; a swelling of the left testicle and a cicatrix of the penis aroused a suspicion of syphilis; later epileptiform attacks occurred. Under iodide of potassium the tumor of the testicle became smaller and the amount of urine markedly diminished, although hemiplegia of the right side, aphasia, and total anæsthesia appeared later.

I once observed a case of gumma of the medulla oblongata (on the calamus scriptorius), in a man forty-two years of age, who had acquired syphilis fifteen years previously. About two years previously ulcers had formed on the left leg, for which gray ointment was used. Eight days before the patient came to my clinic, he complained of headache on the left side and attacks of vertigo. On admission the pupils were found moderately contracted, somewhat more so on the left side, and reacted only sluggishly to light and accommodation; there was also a slight paresis of the right facial. The motor power of the left arm and leg was weakened, moderate ataxia was present, the patellar reflex was increased, and there was clonus of the foot on the left side; the patient swayed on closing the eyes, his gait was straddling and uncertain; with eyes closed the patient deviated to the right in walking; over both lungs a dry rattling was heard, the heart and arteries did not present anything abnormal; the pulse was 70 to the minute, and the respirations 18. On the left leg, besides scars and pigmentations, there were deep ulcers covered with dirty granulations and having a sharp border. Iodide of potassium was administered and a proper local treatment of the ulcers was instituted. The headache increased, slowing of the pulse and vomiting appeared and became worse in spite of increased doses of iodide of potassium. Disturbances of deglutition also appeared, and nutrition had to be carried on by means of clysmata; at the same time the patient had inunctions of 4 gm. of unguentum cinereum and received four Pravaz syringefuls of a forty-per-cent. solution of iodide of potassium subcutaneously. At the end of the second week the patient was seized with a suffocative attack accompanied by tonic spasms; the pulse had fallen to 52 beats in the minute. Gradually his appearance again became brighter, vomiting ceased, and after three weeks the nutritive clysmata could be discontinued. On account of the presence of salivation the third course of inunction had to be stopped, but iodide of potassium was again given by the mouth. Improvement continued hardly a week when headache, vomiting, and difficulty in deglutition again appeared, and necessitated the employment of nutritive enemata, together with subcutaneous injections of the iodide. In the fourth week the suffocative attack was repeated; over both lungs numerous coarse râles could be heard. On the evening of the following day respiration suddenly ceased (without any previous notable symptoms), the patient became cyanotic, consciousness was abolished, the pulse being slow but regular. After

the induction of artificial respiration for ten minutes, the patient rallied and began again to breathe. He died, however, later on during an attack of asphyxia. The post-mortem examination revealed a gumma of the medulla oblongata at the calamus scriptorius, and also hyperæmia and œdema of the lungs.

Leyden and Th. Rumpf report cases which, clinically considered, ran their whole course under the picture of a bulbar paralysis, but which were cured by antisyphilitic treatment. In these cases our diagnosis will be usually of a syphilitic affection of the nerve nuclei within the medulla oblongata.

While we have so far discussed the syphilitic affections of the meninges, the adjacent parts of the brain, and the cranial nerves, we shall now study the syphilitic lesions which are localized within the brain substance. We have here especially to consider the corona radiata and the neighborhood of the central ganglia, as well as the substance of the cord.

As already previously mentioned, the fibres run from the cerebral cortex through the *corona radiata* and through the internal capsule. The position of the internal capsule between the large basal ganglia is the reason why affections of the latter also involve the former either directly or indirectly. Pathological conditions of these parts will therefore, as a rule, lead to a much more extensive paralysis, in which, contrary to what happens in affections of the cortex, symptoms of irritation will be absent.

As regards the anatomical character of these syphilitic lesions, it may be stated that diffuse gummatous infiltrations are hardly ever seen, and circumscribed gummata also are rare, contrary to what we find in the cortex. On the other hand, softening and hemorrhages—as a result of the repeatedly mentioned affection of the vessels—are observed in these localities more frequently than in the cerebral cortex.

Such findings are testified to by numerous observers. Since O. Heubner has made us more closely acquainted with syphilitic affections of the cerebral arteries (see above), communications in this line have been frequently made.

If the affection involves the neighborhood of the *central ganglia*, the symptoms depend especially on the size of the focus. From the nearness of the internal capsule, the latter, as we have already seen, will in a few cases either be directly involved in the morbid process, or at least will suffer from the pressure of the gummatous tumor.

That affections of the cerebral ganglia need not produce any focal symptoms, if the lesions do not encroach on the motor tracts, above all the internal capsule, is proved by a case of Rosenthal, who found

a syphiloma the size of an almond on the first and second joint of the left lenticular nucleus, with an intact internal capsule. This patient, a woman, who had become demented during the last two years, did not present to the time of her death any motor irritative or paralytic symptoms.

Th. Rumpf regards syphilitic affections of the nervous system as granulation tumors, which proceed in every case from the vessels; and indeed we are dealing with syphilitic infiltrations of the connective-tissue capillaries in the diffuse gummatous processes as well as in the circumscribed gummata, while syphilitic arteritis is based on infiltration of the capillaries of the vessels (vasa vasorum). As we have seen above, these two conditions are quite frequently combined; that is to say, affections of the cerebral vessels are often enough found accompanying a diffuse gummatous meningitis as well as circumscribed gummata of the brain or its meninges.

Occasionally the syphilitic disease of the vessels is so pronounced that we are justified in devoting a few lines to it especially. In syphilitic affections of the cerebral vessels, the symptoms will vary according to the degree of the affection and the possibility of the removal of the obstruction to the circulation. As we know, the basal area is supplied by terminal arteries, while in the cortical area the richly anastomosing branches of the vessels render it possible that a certain area may receive its blood supply through the collateral circulation. Another diversity is found in the degree and extent to which the vessels are diseased. A moderate change in their walls may, it is true, cause no symptoms, but when the affection involves larger areas or attacks several vessels, the existing disturbances may probably be dependent on demands made on the cerebral powers which at times are greater than these can perform. In progressive disease of the vessels, the lumen becomes smaller and smaller, the circulation weaker; finally the lumen of the vessel is completely obliterated, or the occlusion is suddenly produced by a thrombus, as a result of the weak blood current. What will now happen will depend on the possibility of an equalization of the disturbance which has occurred; a closure of the terminal arteries causes ischæmia and produces unavoidable destruction (softening) of the cerebral area under consideration.

Quite a number of general cerebral symptoms are natural to syphilitic affections of the vessels as well as to those of the brain, previously described. Especially to be noted are headache and vertigo, insomnia, and mental irritability, loss of memory, as well as a general mental deterioration; occasionally a sensation of crawling or some other sensation is felt one or two days preceding the attack in

the part which later becomes paralyzed (Gowers). Hemiplegias and hemipareses are frequently observed; often they appear suddenly without loss of consciousness; or they are preceded by an apoplectiform attack. At one time the paralysis disappears again quite suddenly, at another it only gradually subsides. Occasionally hemianæsthesia, aphasia, and hemianopsia due to a central lesion occur (H. Oppenheim). Marked paralysis of the cerebral nerves, which so frequently accompanies basilar meningitis, is seldom met with in uncomplicated syphilitic arteritis. If the occlusion of the vessel is only partial, the inconstancy of the symptoms, their changing character, which is so characteristic of lues, stands out prominently. The syphilitic diseases of the cerebral arteries are, as we know, especially characterized by the vacillating character of the cerebral symptoms. In all probability it is due to the changing blood supply of individual portions of the brain that paralysis, disturbances of vision, etc., suddenly make their appearance and then again disappear just as rapidly, to return once more.

In special cases the course will vary, as has been repeatedly remarked, according as the vessels of the cortex or of the base of the brain are the principal seats of the disease. When the arteries at the base are affected, symptoms arise which are caused by softening foci in the area of the great cerebral ganglia, or bulbar symptoms occur when affections of the basilar and vertebral arteries have involved the pons and medulla oblongata. When syphilitic arteritis has led to the formation of an aneurysm, disturbances are to be expected similar to those occurring in the presence of a tumor of the same part. In the further course occlusion of the lumen of the vessel by thrombi or emboli may come on, and the symptoms already described are added. As a rule, however, these aneurysms burst, cerebral hemorrhage takes place, and as a sequel either an agitation and compression from the hemorrhage, or lowered or a total loss of nutrition of the respective portions of the brain result.

A very strong argument in favor of the syphilitic nature of the affections of the cerebral arteries, as of cerebral lues in general, we find in the early age of the patient. Gowers mentions among his patients one of twenty-one years. In persons on the other side of the fifty the possibility of senile changes of the arteries must be taken into consideration. Among fifty cases examined in this relation by Gowers (twenty-one to forty-five years of age) the affection appeared in one-quarter during the first two years after infection; in the rest the intermediate period covered, in one case each eighteen and nineteen years; in one case the attack came on six months after infection.

Occasionally the foci affected confine themselves to very small

areas; in the majority of cases, however, extensive morbid changes are present in cerebral lues. This is very easily explained, for the various syphilitic affections of the brain, which have been specially described, quite frequently occur in conjunction with each other, as has already been mentioned. A syphilitic arteritis particularly is very frequently found accompanying diffuse as well as circumscribed infiltration. Extensive disease of the brain as a result of lues will also clinically make its presence known in a corresponding manner.

In quite a number of cases of cerebral lues, the spinal cord also has been found affected; basilar meningitis syphilitica especially is frequently conjoined with a spinal meningitis of the same kind. As might be expected, there are then added to the cerebral symptoms others referable to the spinal cord. The cerebral symptoms, however, are usually so much the more pronounced that the spinal symptoms are relegated to the background. Occasionally the involvement of the spinal cord is marked by more or less characteristic symptoms, to which belong Gerhardt's "triplegia" (occurrence of hemiplegia and paraplegia at the same time), paralysis of the sphincters, a girdle sensation, knee-phenomena, paræsthesiæ, and others.

The difficulty of diagnosis may, however, be greatly increased by the variability of the localization and of the processes themselves, and, indeed, it may even become insurmountable.

Finally, we would also point out that in many cerebral affections, especially the psychoses, anatomical changes within the central nervous system cannot be discovered with our present methods of examination. Thus Heubner has tabulated eleven minutely reported observations in which, in spite of the presence of grave cerebral symptoms (in syphilitics), the brain was found to be perfectly normal. On the other hand, even extensive syphilitic tumors may be present without declaring themselves by any marked symptoms during life.

'In a fairly large number of observations only general cerebral symptoms appeared, to which focal symptoms were added only after a long period, or not at all.

As the lightest type of this form of the affection may be mentioned the meningeal irritation described by me (see above). Headache, occasionally accompanied by marked neuralgias, vertigo, dulness, increased irritability, disgust or disability for mental work, are more or less marked here. Very frequently these patients show on ophthalmoscopical examination irritation of the retina and choroid (even presenting the picture of an inflammation). Occasionally there is a difference in the size of the pupils or sluggish pupillary reaction to light. A slowing of the pulse to 40 beats in the minute has also been observed by me.

In other cases again I have observed the occurrence of epilepsy in the course of a beginning constitutional syphilis. In one case there was a marked aura (as though the left upper arm were constricted) in individuals who had previously no disturbance whatever of the nervous system, and were also free from any hereditary taint. Attacks of hysteria and hysteroepilepsy have also been observed by me now and then, during the presence of the primary skin syphilides, in otherwise perfectly healthy, robust girls. After antiluetic treatment these symptoms disappeared.

F. Korányi observed in a man thirty-four years of age, suffering from a fresh skin syphilide, attacks of hysteria, disturbance of the intelligence, increased sensation of hunger, and a hyperæmic condition of the head; all these symptoms were dissipated by a course of antisyphilitic treatment. K. Laufenauer observed in two individuals, four and seven months after infection, maniacal attacks, on the one hand accompanied by conditions of depression, on the other by illusions of grandeur, and cured them by injections of corrosive sublimate. Similar cerebral disturbances may even usher in constitutional lues. Thus, a man was admitted to Berthier's section who was seized a few weeks after infection by violent paroxysms of anger, delusions, etc., and it was not until twenty days later that roseola and pharyngeal catarrh made their appearance.

In the later stages of lues also, sometimes years after infection, epilepsy may be the only prominent brain symptom; at other times there will be delirium, maniacal excitement, disturbance of the intelligence, and psychic changes which in addition to gummata of the skin, the mucous membranes, bones, etc., dominate the disease picture. We shall be the more justified in referring the cerebral affection to syphilis when previous infection has taken place, the less we are able in a special case to discover other etiological factors.

It should not be overlooked, however, that syphilis may also attack persons who are either afflicted with a neuropathic taint, or whose nervous system has at some former period received an injury. It stands to reason that under these circumstances an added lues may provoke hysteria, epilepsy, and many other cerebral disturbances. On the other hand, as I must assume according to my experience, injuries which are received by a person infected with syphilis may excite the development of grave lesions of the nervous system. Although we also find cases which run an acute course, it is the rule that cerebral syphilis runs a rather chronic course; yet a very slow course rather excludes lues of the brain. Occasionally certain prodromes (headache, vertigo, etc.) continue for a long time, or a circum-

scribed paralysis persists for many months, until the sudden appearance of grave cerebral symptoms causes a speedy change.

The manifold alternations in the appearance and disappearance of paralytic conditions have already been repeatedly discussed. Syphilis of the central nervous system is a very common form of the disease. It is probable that the frequency of cerebral syphilis has increased in our day, and that its increase is connected with the excessive brain-work, which is forced on us by the great struggle for existence. As a matter of fact, several authors take the view that mental exertion predisposes to syphilis of the nervous system. Other conditions of depression and exaltation, such as trouble and worry, or excesses in baccho et venere are liable to become a cause of cerebral localization in the syphilitic. Beside these factors we must also ascribe to individuals who have an hereditary taint of nervous diseases a special predisposition to syphilitic affections of the brain.

It is quite probable that syphilitic affections of the brain run a much more favorable course than those due to other causes, for the reason that when the process is not yet far advanced a retrogression may be expected, and that they are, therefore, more successfully treated than other cerebral affections. It should not be forgotten, however, that iodide of potassium sometimes effects a marked improvement in cases of non-luetic tumor of the brain. We must not, however, be led to entertain an excessive feeling of security; for we must always keep before us the fact that the longer the symptoms (paralysis, etc.) last, and the more frequently they recur, the less favorable is the prognosis, not only as regards a return to the former condition, but also as regards the life of the patient. We shall therefore be obliged to record, together with a few cases in which the symptoms gradually improved up to a certain degree, others in which the paralysis increases more and more, or the mental faculties degenerate into idiocy, or in which delirium passes into general paralysis and the patient dies in deep coma. In other cases, again, there are complications, such as hypostases of the lungs or a septic condition starting from a bedsore, which may destroy life.

The syphilitic affections of the brain, as we have already said, usually run a chronic course, but we also observe at times, especially in syphilitic psychoses, that the process very rapidly passes into its final stage.

The symptoms referable to other organs will vary greatly according to the period in the course of the disease at which the brain has been attacked.

But many cases are on record in which no positive general symptoms of syphilis have preceded those of localization in the central

nervous system, or in which no changes whatever characteristic of syphilis could be found in any other part of the body. Engelstedt found the nervous symptoms of syphilis alone in twenty cases out of forty-one, and Chvostek in ten cases out of twenty-one. In cases of this kind we are forced to pay greater attention to the clinical symptoms and previous history and also to the success of antisyphilitic treatment in judging of the central affection. The fact was and is still emphasized frequently by some as characteristic of syphilis of the central nervous system that these lesions are developed in the great majority of cases during the later stages of syphilis. Experiments in that direction have taught us, however, that affections of this kind make their appearance as a rule during the first few years, that they are also met with in the early stages of syphilis, and occasionally even usher in the constitutional period of the disease. In certain cases cerebral syphilis, by reason of its early appearance and the gravity of its symptoms, may be justly designated as precocious and malignant.

General Paresis.

We have had occasion to remark several times that cerebral lues may, though rarely, cause psychic changes. One of these psychoses (progressive paralysis, dementia paralytica) should be especially mentioned, for the reason that syphilis plays a more prominent rôle in this affection than do all the other etiological factors taken together. It is not to be doubted that mental overwork and other injurious and irritative conditions may be a cause for the development of paralysis. The fact, however, that syphilis is found very frequently, more frequently than all other conditions in the antecedents of this disease, should not be overlooked. Among the many authors who have subjected this subject to a close investigation, we will mention only E. Mendel, who demonstrated the previous existence of congenital lues in 109 cases of dementia paralytica out of 146 cases (hence in 75 per cent.), while he found syphilis to have preceded primary mental disturbances in 18 cases only out of 101. Similar figures and even larger (up to 90 per cent.) have been given in later works of other observers (Emanuel Regis, F. Bonnet, Ch. Geill, Emil Haugberg, and many others). I may be allowed to remark here that I have found distinct symptoms of a still existing lues in three paralytics. In a fourth case I observed the paralysis developing under my very eyes four years after infection, and a long-continued antiluetic treatment brought an amelioration which could not be denied.

Corresponding to the less frequent occurrence of syphilis in women, especially in those in better circumstances, dementia is also only very

rarely observed. R. v. Krafft-Ebing says that when young women under the age of thirty are attacked by paralysis, syphilis will as a rule be found to have preceded it. Paralysis in young persons should always excite a suspicion of acquired or hereditary lues; and indeed most cases of paralysis juvenilis or puerilis have been met with in just such cases. On account of the undoubted importance which lues possesses in the etiology of dementia paralytica, it will not be out of place to present a brief clinical description of this psychosis.

Symptoms.—Loss of memory and intelligence are the most prominent symptoms, and in addition we find increased irritability, frequently alternating with apathy; immobility of the pupils and disturbance of the speech are very characteristic of the disease. Paralysis (originating in the spinal cord) is rarely absent. Frequently with or without loss of consciousness a hemiplegic, monoplegic, or aphasic attack comes on—the paralytic attack; the paralysis sometimes rapidly disappears, again sometimes it persists for hours or days. Aside from these apoplectiform attacks, epileptiform attacks are also observed. Repetition of such attacks is not infrequent. Although occasionally quite noticeable remissions occur, improvement is never long continued, and the progressive course of the disease leads inevitably to permanent paralysis and total idiocy and ends, as incurable brain diseases in general, after a few years (in rare cases even after a few weeks) in death. Dementia occurs most frequently in individuals between thirty and forty years of age, and then four or five years after syphilis had been acquired. Cases have, however, also been reported in which infection had taken place only two years previously, and others in which twenty years had elapsed since the syphilis was acquired.

Anatomically this paralysis, no matter whether in a specified case syphilis had occurred previously or not, is marked by atrophy of the substance of the cerebral cortex, especially in the frontal portion and a loss of the nervous elements. G. Kjellberg, who asserted a relationship between this form of paralysis and syphilis as early as 1863, found the same changes present in the brain as those that occur in lues. According to E. Mendel, however, we are unable to demonstrate anatomically that interstitial encephalitis has a syphilitic basis. Syphilis has by some been said to increase the disposition to paralysis (Mendel), by others to decrease the resisting power of the central nervous system in general (Meynert). It is my belief that the meningeal irritation, demonstrated by me to exist in the early period of syphilis, although the symptoms as a rule again disappear entirely, may, nevertheless, leave behind such changes in the pia mater and the cortex that a *locus minoris resistentiæ* is formed, or it is

even possible that traces of the specific virus may have remained behind causing pathological changes in after years by being stimulated to propagation in some manner.

Exquisite luetic changes are as a rule not found in this paralysis, although some authorities have held that the anatomical character of cerebral atrophy in dementia paralytica shows evidences of a relation to cerebral lues, or that it even presents a complete resemblance to it. "In addition to the circumscribed luetic processes of the gumma and encephalomalacia," writes Meynert, "the existence of a diffuse infiltrated luetic process appearing under the picture of a progressive paralysis cannot be denied, and it corresponds through easy transitions to the anatomical picture of progressive paralysis."

Obersteiner asserts that there is a direct connection between syphilis and dementia paralytica, notwithstanding that he found a history of syphilis in only 33.7 per cent. of his cases. He sees a relationship to the other lesions of syphilis in the inflammatory process which is present in progressive paralysis and which runs a slow course, attacking the pia and cerebral cortex and finally leading to sclerosis and atrophy. Arguing from this pathological similarity he places dementia paralytica among the later forms of lues. Joseph Adolph Hirschl, after a very interesting analysis of the factors which come under consideration here, reaches the conclusion that "this paralysis is to be looked upon as a later form of syphilis, as an encephalitis syphilitica" the issue of which is in syphilitic cerebral atrophy. The opinions of authors as to the manner in which lues is related to dementia paralytica still diverge, it is true, but most of them agree that these relations are certainly present in a very eminent degree. A. Fournier also, who includes general paralysis among the parasyphilitic affections, is firmly convinced of its relation to syphilis.

Cerebral Neurasthenia.

Finally, we will study cerebral neurasthenia, which in our day is such a common affection. It cannot be denied that everything which affects the brain injuriously, whether mental exertion or diseases which have involved the central nervous system, whether intoxications or traumatisms, may play a rôle in the etiology of this condition. From this point of view it may be possible that syphilis, which as we have seen usually excites at first a meningeal irritation, may become the cause of neurasthenia. Those individuals seem especially threatened who are congenitally predisposed to functional nervous disturbances. If we consider, furthermore, that syphilis in itself, partly on account of the moral depression which it produces,

partly through disturbance of the general condition due to an organic cause, is a debilitating factor in the development of neurasthenia, we may see how much more active a cause it may be when other injuries of the nerve centres accompany it.

Syphilis may injure the nervous tissues not alone by its well-known pathological tissue changes, but also by means of the products of metabolism of the contagium, the toxin. We ought always to bear this possible etiological relationship in mind, since we have in fact succeeded in individual cases, by means of a thorough antiluetic treatment, in permanently curing patients infected a long time previously, who had been for years treated unsuccessfully for neurasthenia with all known methods.

There is still another form of neurasthenia to be considered which, although due to syphilis, is not material but psychic. There are individuals who, with the knowledge of once having contracted syphilis, are unable to get rid of the thought of a continually threatening danger, even after they have undergone proper treatment and have never had any further signs of syphilis. These patients use all their endeavor in searching for syphilitic symptoms. If they discover a harmless pimple, if they feel the slightest bodily discomfort, they rush at once to their physician; and after having been quieted by him they will remain satisfied for a short time only, and will then again fall a prey to their former anxiety. Laboring under the torturing suspicion that his syphilis has not been cured, this troubled individual goes from one physician to another, even undertaking long journeys in order to consult some well-known specialist or to visit certain mineral springs.

We are dealing here with a form of neurasthenia which belongs to the nosophobias, and is specially known as syphilophobia. According to Paul Kovalevsky *syphilophobia* may even produce mental disturbances. "Cases of this kind generally present the character of hypochondria with delirium of syphilitic affections. These patients frequently present a condition of great excitement and fall into a state of active melancholia. They may become dangerous to themselves as well as to those about them."

While we are dealing in the syphilophobic with a patient who wants continually to be treated for syphilis, suffering, therefore, so to speak, from an appetite for mercury, we have in the *hydrargyrophobic* a neurasthenic who is day and night torturing himself with the thought that the mercury which he has been taking, be the quantity every so small, has turned to a never-ending source of new affections. Every change of the skin and mucous membranes, be it ever so faint, slight rheumatic pains in the bones and joints, conditions

really present and all sorts imagined are attributed to mercurial poisoning. These patients are also troubled with a continual restlessness, and know no other thought than how to obtain remedies which will relieve them of the imagined plus quantity of mercury.

We must not, however, overlook the fact that an energetic antiluetic, especially an active mercurial treatment continued for years, may under certain conditions actually induce neurasthenia and other grave nervous accidents, as we shall mention when discussing hydrargyrosis. I have repeatedly, in the course of my experience, observed grave neurasthenic symptoms, which on account of their disturbing character led one to fear the development of cerebral lues, begin to improve and even disappear, when on my advice the patient was sent to the mountains, the seashore, or elsewhere, in place of taking the different mercurial and iodine preparations.

We may also remark that occasionally very grave affections of the brain make their first appearance with the symptoms of a neurasthenia. First among these we may mention progressive paralysis, which, as T. Donath also points out, can sometimes be differentiated only by a careful clinical examination. There are, however, also cases of general cerebral lues which for a long period present no focal symptoms and make their presence known only by general cerebral symptoms, such as headache, insomnia, ill humor, a sense of fatigue, etc. We should carefully notice, therefore, whether in the further course of the affection the signs of an organic central lesion are not added to those of lues. A beginning paralysis, or even a light deviation from the normal condition of the pupils, often suffices to justify the suspicion of a grave cerebral affection.

The Spinal Cord.

In comparison with cerebral syphilis analogous affections of the spinal cord are of less frequent occurrence, yet recent observations have shown us that the medulla spinalis is frequently involved in the course of syphilis.

It is not improbable that several nervous symptoms occurring during the generalization of syphilis are to be referred to conditions of irritation of the spinal cord, perhaps of the sympathetic also (v. Rinecker). In some cases the symptoms in the beginning of the generalization of syphilis are very marked. The patient complains of pain and paræsthesia of the legs, accompanied by a feeling of debility, so that the individual attacked is unable for some time to use his lower extremities in the same measure as formerly. From the fact that this trouble appears during the time of the first erup-

tion of syphilis, and as a rule can rapidly be made to disappear under an antisyphilitic treatment, we are probably justified in assuming the presence of hyperæmias or slight infiltrations in the spinal cord or its membranes as a cause of these symptoms. I have designated this condition *spinal meningeal irritation*. Under unfavorable circumstances a spinal meningeal irritation may increase to a distinct meningitis or meningomyelitis spinalis; Magnus Möller reports an unequivocal case of this kind.

A. Jarisch has reported a case of increase of the skin and tendon reflexes in recent syphilis. Under exactly the same conditions, E. Finger was able, independent of Jarisch, to demonstrate in certain cases quite a marked increase in the skin and tendon reflex irritability immediately previous to and at the time of the appearance of the exanthem. This was soon followed by a decrease of the reflex irritability frequently to below the normal, and in some cases even to complete absence, after which it slowly and gradually rose again to normal, which it did not reach as a rule until several weeks after the disappearance of the exanthem.

Occasionally *spinal meningitis* accompanies syphilitic periostitis of the vertebræ. This is, however, only rarely the case, for the reason that the layer of fat between the vertebra and the dura to some extent protects the latter. Affections of the dura alone, aside from this, occur but rarely. As a rule the disease arises in the pia mater, and then leads to a matting together of the meninges. The process usually includes the nerve roots as well as the spinal cord.

Spinal meningitis, as well as cerebral meningitis, is marked at times by a gelatinous, at times by a fibrous vegetation, consisting of connective tissue, rich in blood-vessels, densely packed with cells. Here and there small gummatous foci are found scattered in the new growth. An important rôle must be ascribed to the changes in the blood-vessels (Rumpf, Oppenheim, Siemerling, and others). The diffuse form of meningitis is more frequently found than the circumscribed form; but it is generally more or less limited in its extent, most frequently involving only the dorsal portion of the cord. It may, however, be found extending over the greater portion of the spinal cord.

On cross section also the inflammation is rarely found distributed evenly over the whole surface, but frequently it seems to be more intensely developed in the region corresponding to the posterior sulci (Oppenheim).

The adjacent portions of the spinal cord are hardly ever spared. The lesion extends from the pia into the outer portion of the spinal cord, or offshoots dip down into the latter (Oppenheim, Siemerling),

and this leads, as a matter of course, to greater destruction. As a result of the luetic disease of the vessels, which is hardly ever absent, foci of softening are formed in the spinal cord, as well as in the brain, and in the neighborhood of these capillary hemorrhages are frequently found.

Adolph Jarisch found among the lesions of spinal syphilis atrophy of the ganglionic cells, homogeneous foci in the tissue of the anterior horns and in the commissure, hemorrhages into the tissue of the commissure and the anterior horns, and a sclerosis of the gray substance.

Circumscribed gummatous affections of the meninges or of the spinal cord itself have been found but rarely. *Gummatous meningitis* causes a callous degeneration of the dura mater, which leads, according as the gummatous process is most pronounced on the external or on the internal surface, to adhesions with the vertebral periosteum, or between the pia mater and the contiguous portion of the spinal cord. This syphilitic false membrane occurs as a rule only in circumscribed localities.

The *gumma of the spinal cord* generally takes its origin from the meninges, which become adherent to each other and to the cord, forming a jelly-like, dry, cheesy mass. Infiltrations of this kind occur in but one or only a few foci, or else they are distributed in the form of miliaria over a large territory.

Individual affections of the spinal cord in the form of single or multiple gummata are still more infrequently found. As a result of *disease of the vessels*, we may also find an uncomplicated affection of the spinal cord. M. Möller has observed a case of this kind, in which there occurred endarteritis obliterans, and also a hyaline degeneration of the vessels.

Finally, we have to mention that in the case of syphilitic affections involving the nerve roots and the spinal cord in such a way as to cause an interruption of the conducting tracts leading from the ganglion cells (the trophic centres), there occurs, as in lesions of other nature, a secondary degeneration which is a descending one in the motor tracts and an ascending one in the sensory tracts.

Syphilis of the spinal cord is frequently complicated with syphilis of the brain, as has been demonstrated many times on the post-mortem table.

Symptoms.

The symptoms of syphilis of the spinal cord cannot be grouped into one uniform picture, for they vary according to the location and intensity of the morbid process. Corresponding to the meningomy-

elitic character of spinal lues, symptoms on the part of the spinal cord are also present in addition to the meningitic symptoms, as we know from most of the observations which have been published. We shall have occasion later to note some isolated cases in which this complication was not present. In the majority of cases, the process extends over a large portion of the spinal cord, even though it has started in a limited area.

A certain stiffness of the spinal column and a heaviness in the extremities, neuralgias in certain parts, and girdle pains or paræsthesiæ are frequently the first symptoms noticed in syphilis of the spinal cord; with this the sensibility is usually but little diminished or only for certain kinds of sensation. After the process has attacked the conducting tracts, sensory or motor pareses will of necessity follow, which, according to the magnitude of the disturbance, will involve only circumscribed areas of sensation, possibly single groups of muscles, or else extensive areas.

Paralysis, when the anterior roots (or the gray substance of the anterior horns) are diseased, is accompanied by atrophy of the muscles involved, and is flaccid in form; or the paralyzed muscles are in a spastic condition, and then less frequently become atrophic. Disturbances of the bladder and of the rectum, as well as a lowering of the tendon reflex, occur quite frequently. The diminution of sensibility does not as a rule keep pace with the other disturbances, as sensory impressions are longest observed. The symptoms, which require weeks and months for their full development, may decline of their own accord gradually or after rational treatment, or, what is more often the case, they rapidly progress as the morbid process advances. According to the extent of the lesion in the cross-section, hemiparesis or paraparesis will be observed. If the latter is present it is usually less marked on one side than on the other. We should, however, note that in the rare cases of isolated gummata we may have paralysis in different parts of the body corresponding to the independent root areas involved in the morbid process.

The symptoms which correspond to the varying seat of the lesion are frequently quite typical. If the *dorsal* or *lumbar cord* is the seat of the gumma, we shall find more or less complete paralysis in the region of the abdominal muscles and the intercostals, or paraplegias of the lower extremities; and according as the morbid process continues to advance or is arrested we find either a paralysis of the sphincters only or also of one of the muscles supplied by the upper spinal nerves. But even in those cases in which the paralysis involves only the lower extremities and the sphincters, unless retrogression of the lesion occurs, we must look for an ultimately unfavor-

able issue, brought about by the inevitable complications in the form of cystitis and decubitus.

If the cervical portion is the seat of the disease, pain, paræsthesia, and stiffness of the neck and the upper extremities are usually the first symptoms, and the lower extremities will be attacked only later. According as the muscular tissue of the thorax and the diaphragm is earlier or later attacked by the paralysis, dyspnœa and attacks of asphyxia will complicate the disease picture. At other times the symptoms may be noted on only one side of the body, and then we see first the upper and then the lower extremity attacked, the extremities of the other side not being affected until after the lapse of some days. In still other cases of affection of the cervical cord the symptoms may present themselves in the shape of an ascending paralysis, the paraplegic attacks occurring at first in the legs, then in the sphincters and the muscles of the trunk, and only later in the upper extremities and the respiratory muscles.

It goes without saying that the disturbances will be the more extensive the higher the lesion is situated in the spinal cord. The course of the disease will be even more unfavorable, as disturbances of respiration from paralysis of the respiratory muscles are added to the dangers already existing in the shape of cystitis or decubitus. This respiratory paralysis may lead to dangerous centres of inflammation and gangrene of the lungs; or diaphragmatic respiration may suddenly become impossible through paralysis of the phrenic nerve, and then the patient is asphyxiated.

Even the grave forms of syphilis of the spinal cord, however, afford us some hope, since more or less marked improvement is possible. The symptoms in that case improve in consequence of the disappearance of the paralysis first of the respiratory muscles and those of the trunk, then of those of the upper extremities, of the sphincters, and finally of the muscles of the legs. With this it is observed that if the paralytic symptoms have been more severe on one side of the body than on the other, improvement takes place unevenly, so that even when improvement continues, a weakness of the muscles, painful stitches, and other abnormal sensations will remain behind in the side which was most severely affected.

It goes without saying that gummatous processes, even when they improve, cause irreparable changes (degenerations) in consequence of which certain disturbances remain permanent.

Syphilis of the spinal cord, as a rule, develops only gradually and frequently accompanies the same affection in the brain (Siemerling), so that cerebrospinal lues seems characterized by a descending course of the process (R. Jürgens, Oppenheim). The spinal affection may,

however, develop acutely, and cases have also been observed in which the lesion progressed from below upwards.

An advance of the disease in successive exacerbations is quite characteristic of syphilis of the spinal cord, but it is also characteristic of *multiple sclerosis*. The latter is, however, sufficiently characterized by the pathognomonic tremor (which affects the muscles only when in motion, not when at rest), the hesitating speech, and the nystagmus, as well as by the absence of symptoms of meningeal irritation.

Quite frequently, also, we find a changeableness, fluctuation, of the symptoms, as already mentioned, in *meningomyelitis syphilitica*. This is especially noticeable in the patellar reflex—the reflex being absent at one time and present again a few days later. This symptom, first recognized by Albrecht Erlenmeyer, has been since then demonstrated by others (Siemerling, Oppenheim). Paraplegia rarely makes its appearance suddenly; when it does we are constrained to assume the presence of an endarteritic process, which has led to thrombosis or hemorrhage.

In only a few cases does syphilis of the spinal cord run its course altogether under the picture of an acute, subacute, or chronic *myelitis*. In several cases the symptoms corresponded perfectly with those of *tabes;* absence of the patellar reflex, lancinating pains, ataxic gait, immobility of the pupil, disturbances on the part of the bladder, gastric crises, etc., remind one so much of tabes that Oppenheim gave to this symptom complex the term pseudotabes syphilitica. We are dealing in these cases with a meningitis spinalis syphilitica which has especially affected the posterior columns and the posterior roots.

Irritation of the spinal meninges, to which I called attention many years ago (in 1880), represents the lightest form of the affection under consideration. It may be encountered early in the course of the constitutional disease. Concerning this the reader is referred to what has been previously said, and I will add that my observations have also been corroborated by other clinicians. Occasionally the meningeal irritation passes into a meningitis. Thus, S. Goldflam observed in a man forty years of age, during the early constitutional stage, a meningeal affection of the cervical portion accompanied by violent pains radiating to the arms and stiffness of the neck, besides which there were tenderness on pressure over the spinous processes and hyperæsthesia of the skin of the neck and of the interscapular space. Antiluetic treatment caused partial improvement. Occasionally meningomyelitis appears early, and in a severe form. In the majority of cases a syphilitic meningomyelitis affects the thoracic and lumbar regions.

In a case recorded by C. Eisenlohr the lumbar cord and the cauda equina seem to have been affected.

A man, 30 years of age, who had acquired syphilis eleven years before, suffered in late years from disagreeable sensations in the region of the anus, and from weakness of the legs; later on paralysis of the rectum and bladder, paralysis of the right leg, paresis of the left leg and reduced sensibility of the skin, more on the right than on the left side, appeared. When mercurial treatment was begun moderate improvement followed, but later on the condition of the patient again became worse. The post-mortem examination revealed adhesions of the dura to the pia reaching from the tenth dorsal nerve to the end of the sac, on its posterior surface; the pia was turbid, gelatinous, and thickened. The nerves of the cauda equina seemed firmly bound together by bands of connective tissue which came from the pia; the posterior roots were of a brownish-gray color; the posterior columns were the seat of a degeneration gradually diminishing from below upwards. In individual cases this meningitis affects only the cauda equina.

Delafield describes such a case:

A man 46 years of age, who had been infected five years previously and who complained later on of pain in the limbs, but observed no other symptoms in himself, had suffered for the past two months with progressive weakness of the legs, involuntary discharge of fæces, and some difficulty in evacuating the bladder. On the skull and the right tibia nodes were found. The patient died suddenly from intercurrent erysipelas. At the autopsy the spinal cord seemed unchanged, while a yellow, cheesy tumor the size of a pea was found in the large nerves forming the cauda equina, two inches above its end, which involved several spinal nerves, and to which the dura mater was adherent; two inches lower several nerves were also adherent to each other and degenerated.

In a case which I observed the symptoms pointed to a meningitis of the cauda, which had affected only the sensory fibres (roots). A man, over 60 years of age, who had the misfortune to contract an extra-genital infection, presented cutaneous and subcutaneous nodular deposits soon after the infection became constitutional, some of which broke down. The nervous system had been involved early. The patient felt out of sorts and irritable, he began to look ill, the appetite was lost, and hearing became defective on the right side; diabetes insipidus was also present. An objective examination of the nervous system revealed in general only negative symptoms. Subcutaneous injections of soluble mercury salts, which had been given most irregularly, had at once caused a metallic taste in the mouth and, according to the patient's statement, also muscular tremors. In view of this fact and the inclination of the affection to malignancy, I ordered at once iodide of potassium and decoctum sarsaparillæ inspissatum. During his sojourn in London improvement took place to the extent that the appetite returned, the disposition improved,

and the polyuria disappeared. At about the tenth month of the disease, the patient noticed that as he arose from his armchair his right lower limb, without being useless, was still very clumsy, and had a numb feeling. The right leg had a girdle-like feeling of constriction; the soles of his feet seemed to be absent, the patient losing his slippers without knowing it; the rectum felt as though it always contained a heavy load, but when the patient sat on the closet he was not aware whether he had passed anything or not, until he had inspected the pan; the glans penis felt as though dead, the act of micturition was unaccompanied by any sensation, and the patient could tell that the bladder was empty only by noting that the urine ceased to flow. When I saw the patient again three or four weeks later he still complained of a sort of a furry, numb sensation in the right leg, but the condition had so much improved after a few inunctions that the feet were, so to speak, more aware of the presence of the slippers; the passage of urine and flatus was felt on the left side, on the right sensation was still absent. The objective examination revealed no notable disturbance of sensation. When the patient was touched while his eyes were closed, he was able quite well to localize the point of contact. Letters and numbers which were drawn on the skin with the probe were accurately named. He was able to locate the joints of the toes normally, and the gait with closed eyes was sure; the muscles were not weakened. For a few days the patient had sluggish pupillary reaction. Later the improvement was marked.

An observation by C. Westphal is especially instructive on account of the autopsical findings. A woman 32 years of age, who denied having had any specific affection, complained of pain in the legs and a feeling of fatigue and numbness in them. She also complained of a feeling of bearing down in the rectum which was so severe that she was unable to walk. Gradually she fell into a condition in which the fæces were passed involuntarily and there was difficulty in urination. Later tactile sensation was lost in the neighborhood of the anus, and the act of coitus produced no sensation. A slight falling of the patient's hair was suspicious, as well as the presence of enlarged inguinal glands, a cicatrix in the right inguinal region, and a loss of substance the size of a pea in the right palatine arch. Motion and sensation of the arms and legs were found to be normal. The skin over the lower part of the sacrum was changed into a dry scab. Absolute anæsthesia was present in the skin of the external genitals as far as the border of the mons veneris, in the mucous membrane of the vagina, over the perineum and on the inner surface of the thigh, in the immediate neighborhood of the perineofemoral crease. The lower portion of the skin in the gluteal region and the mucous membrane within the anus were also anæsthetic, so that the patient did not feel the passage of fæces. The anus was not patulous and grasped the finger with moderate force; the bladder was greatly distended, and the patient could pass only a small quantity of urine by straining forcibly. The catheter which was passed could not be felt, and the patient was wholly unaware of the distended state of the bladder. As motor disturbances could not be demonstrated, an affec-

tion of the spinal cord was excluded. A diagnosis was made of a gummatous affection of the posterior roots of the pudendal and coccygeal nerves with involvement of the posterior roots of the sciatic plexus (whence arises the posterior femoral cutaneous nerve). In spite of the antisyphilitic treatment to which she was subjected, the patient died. At the autopsy a gummatous spinal meningitis in the sacral region compressing the roots of the plexus pudendalis was found, and also caries of the sacrum. The spinal cord was found intact, the mucous membrane of the bladder, of the vaginal introitus, and of the rectum was the seat of dirty brownish-yellow infiltrations.

Disseminated neoplasms of the meninges are rare, and rarer yet are *gummata* in the *spinal cord.* Occasionally the morbid changes are especially marked or preponderate in the anterior horns. The atrophic form of the paralysis, the presence of the reaction of degeneration (in which the muscle which is not affected by the faradic current can be seen to react slowly to the galvanic current, while the irritability of the nerve is abolished for both forms of current), the absence of bladder and rectal symptoms, as well as the absence of sensory disturbances or their occurrence to a very slight degree, are important clinical signs of this localization.

In a case treated by myself (in conjunction with Dr. S. Freud), the presence of multiple foci in the anterior and posterior gray substance had to be assumed. A man, about 40 years of age, complained for several months of a weakness in the right hand, a burning sensation having been previously felt in it and in the whole arm; the left foot was weak and was being dragged, and there was also a sort of tickling in the sole of the left foot; the lumbar region had for some time been stiff and bending forward was difficult. At the examination a commencing claw-hand was found on the right side, deep atrophic furrows corresponded to the interosseous muscles, and the thenar eminence was absent. The power of voluntary movement was nearly abolished, and the opposition of the right thumb especially was impossible; the right arm was in general somewhat atrophic and felt cool to the touch; the sensibility, especially the sensation for pain and temperature, was markedly diminished in the whole extremity, but especially in the hand. The same condition was found in the left foot, which appeared narrow and presented very little prehensile play of the toes. The urine could be voided only after some waiting and fell vertically, the bladder having no expulsive force; it was turbid, and the residual urine amounted to from 80 to 100 gm.; the bowels were somewhat sluggish. With the exception of slightly exaggerated patellar reflexes, somewhat more pronounced on the left side, no other disturbances could be discovered. The patient said that he had never to his knowledge had an initial lesion, but on careful inspection there was found on the thigh a cicatrix, surrounded by pigment, such as usually remains after a gummatous ulcer. The patient could only remember a "furuncle," which had

been situated here, and which had been months in healing; later he admitted having had a scaly nodule on the penis, which, however, healed without any trouble. Marked improvement, especially as regards the sensory disturbances, set in after the patient had taken iodide of potassium for a few weeks. A nearly perfect cure resulted in the further course of treatment after subcutaneous injections of a fifty-per-cent. solution of oleum cinereum (thirteen doses, each of 0.05 c.c., or 0.65 c.c. in the course of eleven weeks), and electric treatment of the muscles of the hand only. The left leg became so strong that the patient was able to take three-hour walks and ascend quite steep hills. The bladder emptied itself perfectly, so that no residue could be demonstrated, the urine became perfectly clear. The strengthened small muscles of the fingers and the regenerated thenar were able to perform all movements and developed a normal reaction. Previous to the faradic and galvanic treatment, most of the interossei answered to the faradic as well as to the galvanic current by weak but rapid contractions; the adductor pollicis reacted only weakly and sluggishly to the galvanic irritation, the opponens seemed altogether lost.

The connection of some cases of *progressive muscular atrophy* with lues is probable. Recently Raymond described four cases of progressive muscular atrophy (due to syphilis) of the Aran-Duchenne type. These may be distinguished from the non-syphilitic form by the pain and paresis which precede the atrophy of individual muscles. A. Fournier classes this affection, which does not improve under antisyphilitic remedies, among the "parasyphilitic."

We have also records of observation relating to *spasmodic tabes dorsalis of Charcot*, or *Erb's spastic paralysis*, which a few authors (E. Leyden, Minkowski, Naunyn) refer to a previous syphilitic infection. As a rule sensory disturbances are absent in those affections of the spinal cord which run a chronic course, as also disturbances on the part of the bladder and the rectum; the symptomatic picture is dominated by the spastic paralysis only.

In some cases pronounced syphilitic disease of the spinal cord has produced typical symptoms of tabes. Oppenheim designates these forms *pseudotabes syphilitica*.

We may also mention the symptoms grouped together by Erb under the designation of *syphilitic spinal paralysis*, in which we are dealing with a meningomyelitis of gradual development. In fully developed cases, a spastic gait is present; the patient drags himself along with stiffened legs and by great exertion.

The paralysis is nevertheless slight in degree, and only in rare cases does the weakness of the lower extremities pass into actual paraplegia. In contrast with this, however, the patellar tendon reflex is increased. In spite of the spastic gait, muscular rigidity and

contracture are as a rule present only in a slight degree. In the presence of distinct paræsthesia sensory disturbances are only slightly marked. Weakness of the bladder and impotence are constantly present, muscular atrophy is absent, electrical irritability is present. The nerves of the arms, head, and brain are spared. Syphilitic spinal paralysis makes its appearance comparatively early in the course of syphilis, from the first to the third year, rarely from the sixth to the twentieth year after infection. In a case under my observation, which markedly improved under mercurial treatment, the infection could be traced back seventeen years. The disease shows an undeniable tendency to recovery under antisyphilitic treatment, but we may meet also with grave cases that are incurable or end lethally. This disease picture should be carefully distinguished from the *spasmodic tabes dorsalis of Charcot*, or the *spastic paralysis of Erb*, which has already been mentioned. In a work based on observations in Erb's clinic, Sidney Kuh has collected from the literature numerous cases which correspond to syphilitic spinal paralysis. According to the anatomical researches made in a few cases, extensive infiltration leading from the small vessels (see also Magnus Möller) are found; these affect certain areas of the spinal cord, and present the picture of an acute myelitis in fresh lesions, and of scleroses in older foci. In the longitudinal section the process is found to be localized usually in the dorsal segment of the cord, more rarely in the lumbar, and most infrequently of all in the cervical portion. The focal affection is most strongly marked in the lateral columns, but is also met with now and then in the posterior or anterior columns. The leptomeninges, especially the pia, are thickened and cloudy and are the seat of an arteritis. In older cases the cord on cross-section is seen to be diffusely affected, and the lesion is followed by ascending and descending degeneration.

In rare cases, a multiple syphilitic root neuritis arising from a gummatous meningitis is found. In this case an independent small-celled infiltration of the epineurium of the pia (the peripheral epineurium) makes its appearance in the nerve roots, and this is followed by a loss of the nerve fibres, and the formation of syphilitic products. All the cerebral and all the nerve roots may be attacked by these changes. While, however, the oculomotors and facials are most frequently affected among the nerve roots of the brain, those of the cervical and dorsal portion are attacked by preference in the spinal cord; the involvement may be unilateral or bilateral, and affects now the anterior and again the posterior roots.

The *symptomatology* of syphilitic neuritis of the roots is characterized by the fact that a gradually progressive paralysis is developed

in various cerebral nerves in addition to the symptoms of cerebral lues, or even without them, which paralysis may be recognized in the more favorable cases (as in the facial) as a peripheral one. Furthermore, gradually increasing neuralgias of the spinal nerves and hyperæsthesias of the skin or girdle pains, and as the case progresses, disease of the anterior spinal nerve roots which leads to motor palsies (also peripheral in form), will make their appearance. Antiluetic treatment in these cases has, up to the present, it is true, given very insignificant results.

Tabes.

The number of affections of the spinal cord caused by syphilis is swelled enormously by the great figure which is presented by the cases of tabes due to syphilis. Not only is tabes dorsalis more common than all other syphilitic spinal diseases, but it also occupies the first place among all affections of the spinal cord.

The knowledge of the frequent association of tabes with syphilis is an acquisition of recent decades. Up to that time tabes (consumption of the spinal cord), which was first described in the fifties of this century (Romberg, Wunderlich, Duchenne) as a clinically well-characterized affection, was referred at times to catching cold and bodily fatigue, at times to excesses and mental overwork or to injurious influences of a similar kind. Although Duchenne (of Boulogne) several times noted the occurrence of syphilis in the previous history of tabetics, the honor belongs to A. Fournier of having first made the assertion that tabes was dependent on syphilis. From this time on the study of the etiology of this affection followed a new course, and was so earnestly carried on that a really extensive literature on this subject has grown. A. Fournier, who suggested the causal relation between tabes and syphilis, his belief being based on the statistics of his cases, at once had the support of W. R. Gowers, Vulpian, and Grosset, and later of W. Erb, Oscar Berger, M. Benedikt, A. Erlenmeyer, Voigt, and others. The number of opponents of this view was, however, also quite numerous: Charcot, V. Cornil, Broadbent, L. F. Fulliard, Albert Eulenburg, C. Westphal, M. Bernhardt, E. Leyden, M. Rosenthal, Thomas Buzzard, and others. The two parties were not, however, in strict opposition along the whole series. Only very few said that tabes and syphilis had nothing in common; others again admitted the existence of certain relations; thus Eulenburg counted himself among the "conditional" and restricted adherents of the tabes-syphilis theory. According to Gesenius, F. Hutchinson, and S. Domansky lues only induces a predisposition to tabes. According to Pusinelli syphilis acts as an exciting cause when a pre-

disposition to tabes already exists, and at another time saturation of the body with the poison of lues creates a predisposition to tabes. But even the opponents of the syphilitic theory of tabes agreed that antisyphilitic treatment—that is to say, treatment by iodine or mercury—is curative at times (Domansky, Rosenthal), or at least is justifiable (Westphal). On the other hand, some hold that an energetic inunction treatment is dangerous, even in cases of syphilitic origin.

As time went on, however, the force of the newly collected statistics could not be ignored any longer. A strong impression was undoubtedly produced when A. Fournier reported out of seven hundred and fifty cases of tabes eighty-seven to ninety-three per cent. with syphilitic antecedents. It may seem at first sight, it is true, that this high percentage is due to one-sided material, as the syphilologist is naturally consulted by patients who have previously suffered from syphilis; but this objection is nullified when we see that W. Erb, who was not a syphilologist, found a history of syphilis in eighty-nine per cent. of his six hundred cases of tabes (sixty-three per cent. were suffering with constitutional syphilis). According to the statistics of other clinicians, such as Eisenlohr, Remak, Minor, Strümpell, Rumpf, Labbé, Martineau, and Dejerine we find from sixty to ninety-seven per cent. of tabetic persons who had a history of previously contracted lues. Even those, like L. Edinger and Alessandro Bargherini, who regard the etiology of tabes as altogether different, are constrained to admit that syphilis plays an important rôle in the development of the disease. It should not be forgotten, however, that prominent clinicians like E. Leyden and E. Lancereaux adhere even to the present time to their original opinion that syphilis has no connection with tabes. Most practitioners, however, convinced by the mass of statistical material pointing in this direction, look upon syphilis as playing the most important etiological rôle in tabes, or even, as many maintain (P. J. Möbius, S. Freud, Pierre Marie, H. Oppenheim, and others), the principal rôle. Indeed, all other etiological factors occupy a very subordinate position. Even hereditary predisposition occupies no dominant position in the etiology of tabes, as we find that it is exceedingly rare for more than one member of the same family to be affected, and when this happens it is much more naturally explained by other causes. W. Erb mentions two pairs of brothers, but all of the four patients had contracted syphilis. Furthermore, among Erb's cases the fathers of two tabetic patients had also suffered from tabes, so also in one of Goldflam's cases; but in the latter as well as in one of Erb's cases both father and son were syphilitic. It is also known that tabes generally begins in middle life, and when it has made its appearance in later life, in-

fection with lues has also occurred very late. Erb, Rumpf, Voigt, and O. Berger mention such cases. It is, however, possible that tabetic symptoms may develop more rapidly in individuals who acquire syphilis late in life.

Thus J. Donath (in a personal communication) reports the case of a man, about 55 years of age, who was attacked for a month every evening at the same hour by violent intercostal pains (in the fourth and fifth intercostal spaces) which were looked upon as due to malaria, and for which he had previously been unsuccessfully treated with large doses of quinine. Examination showed contracted pupils, reacting alike, however, to light, paralysis of the right superior oblique muscle, absence of the knee phenomenon on the right side, and diminished patellar reflex on the left. The pain had of late radiated to the right hypochondrium and to both legs; the girdle sensation was felt. With this there was present a maculopapular syphilide on the trunk and extremities, so that infection had probably occurred about three months previously. The portal of entrance could not be discovered. The patient had denied the occurrence of any genital affection, and said he had not had coitus for years. In the course of the following four weeks the pupils became irregular and lost their light reaction. A left-sided ptosis and a right-sided facial paralysis also developed. A course of inunctions rapidly removed the pains, the trochlear and oculomotor paralysis, as well as the skin syphilide, and improved the general condition. Inequality of the pupils, Robertson's and Westphal's symptoms, as well as the right-sided facial paralysis persisted.

The infrequent occurrence of tabes in young men and still more in young girls has its reason also in the nearly exclusive luetic etiology of the disease, and corresponds to the infrequency of acquired lues in early age. Published cases of tabes in the young (infantile or juvenile tabes) have been in patients with hereditary syphilis (A. Fournier, B. Remak, A. Strümpell, W. R. Gowers). For the same reasons tabes is met with in women much less frequently than in men, and where it is found a previous syphilis can be generally demonstrated (P. J. Möbius, Friedrich Friedricksen); or the cases were those of women whose husbands were syphilitic, and in some cases infection by the husband was proved to have occurred (F. Raymond). In the few cases of tabes in husband and wife, both parties were syphilitic in every case (Erb, Voigt, Strümpell, S. Goldflam, and others).

Even though the great majority of authorities are agreed as to the frequent connection between tabes and lues, opinions are still divergent as to the manner of this connection. Some even yet support the view that syphilis merely causes a predisposition to tabes. According to A. Fournier tabes is probably of syphilitic origin, but is not

syphilitic in its nature; for this reason he classes it with the parasyphilitic affections. Möbius considers tabes to be a sequel of lues; Adolph Strümpell also looks upon it as a postsyphilitic affection which rests on an intoxication, and he thinks that the essential rôle is to be ascribed here to the metabolic products of the contagium (toxins) of syphilis. On various occasions since 1884 I have given expression to the opinion that we must take into account, during the course of syphilis, not only the pathological processes caused by the contagium, but also the effects of the products of this contagium. We may, therefore, very well assume that the nervous system may not only be subject to pathological tissue changes, but may also be affected by syphilotoxic influences.

The acceptation of the purely luetic character of tabes would find a powerful support in the coincidence of the affection with manifestly syphilitic symptoms. As a matter of fact, the histories of most cases of tabes do disclose a syphilitic infection, but active syphilitic products are at the same time rarely mentioned as present. In the patients examined by me I was able in only one case to demonstrate marked signs of lues in the skin, bones, etc. The presence of distinctly demonstrable signs of syphilis in an individual justifies one to look upon a diseased focus which cannot be reached by a direct examination (as for example one in the spinal cord) as also being syphilitic. But we must not conclude from the absence of these symptoms that the affection of the spinal cord is not of a luetic nature. In cerebral syphilis also the characteristic change is not uncommonly confined to the brain alone (see above). Nevertheless, we possess records of observation and autopsical findings of tabetic individuals who also had undoubted syphilitic lesions in other localities or in the spinal cord itself (Virchow, Duplaix, Sidney Kuh, Eisenlohr, L. Minor, M. Dinkler).

It stands to reason that great importance should be given to the results of the anatomical examination in judging of the nature of tabes. Although unequivocal syphilitic changes have been found in the spinal cord in a number of well-authenticated observations on tabes, the fact should not be overlooked that in the great majority of cases no marked syphilitic deposits are discovered, but a (gray) degeneration of the posterior columns ending in destruction of the nerve cylinders and proliferation of the glia substance. A few observers earlier claimed that tabes took its origin in the posterior roots, whence ascending degenerative changes advanced in the direction of the cord, and other lesions extended towards the spinal ganglia, accompanied by an atrophy of the axis cylinder and of the ganglia cells (Wallenberg, Oppenheim, Obersteiner, and Redlich).

The work of H. Obersteiner and E. Redlich is worthy of great consideration. These authors demonstrated meningeal changes in the spinal cord in tabes which occur especially in the posterior portion and declare themselves by a chronic tissue hyperplasia accompanied by recent cell infiltration. These changes are most marked in the constricted portion of the posterior roots, at the point where they pass through the meninges; here the degeneration also begins.

Moreover, one or more vessels are also found thickened at the base of the constriction and towards the periphery. As now similar changes occur under the influence of syphilis, namely, chronic inflammation, connective-tissue hyperplasia, and changes in the arteries, we may find here a clew to the understanding of the connection between tabes and lues. The degeneration is only a result of the meningeal and arterial processes.

But in any case we are forced to admit that these meningeal changes do not sufficiently explain many symptoms which usher in or accompany tabes, such as paralysis of the ocular muscles, hemiplegia, and paraplegia. But we should not assume that these disturbances are integral parts of the symptoms of tabes; on the contrary, the paralysis, as Fournier, Erb, and L. Minor insist, rather points indubitably to a syphilitic process and confirms the belief that the tabetic symptoms are also connected with syphilis.

In judging of the syphilitic nature of a disease process, the result of an antisyphilitic treatment is naturally of the greatest importance. We must not, however, overlook the fact that while specific treatment will probably cause absorption of the syphilitic infiltration and thus effect a cure—quite frequently through the formation of cicatrices—it is powerless against destructive changes already caused by cicatricial contraction. If a luetic deposit (let us say in the liver) while healing results in the formation of cicatrices, the lost parenchymatous portion will not be replaced, but compensation is effected by the parts of the liver which have been preserved assuming the functions of the destroyed cells, so that after the specific process has run its course, if it was not too extensive, no marked disturbance of function is left behind. In syphilitic affections of the central nervous system, however, the conditions are essentially different. Here we can hardly expect restitution of or compensation for destroyed nerve elements. From a pathologico-anatomical point of view the formation of cicatrices and callosities is probably looked upon as a curative process, but functionally a defect remains, the effects of which are frequently enough diminished, but hardly ever entirely removed. This is the reason why cerebral syphilis so frequently, or more frequently still syphilis of the spinal cord, even when it runs a favorable course,

leaves behind irreparable changes, now slight, and again most serious. Exceptions to this occur only when, as is assumed of the centre of hearing, compensation is made by the centre of the other side (W. R. Gowers). Thus Ball reports a case in which, in spite of an undeniable lesion of the first (upper) temporal convolution, there was no deafness on that side.

Bearing this in mind, we have no reason to expect that an antisyphilitic treatment, even in an evidently syphilitic spinal affection, will always or even generally effect an absolute cure. Especially must we entertain modest hopes in the case of tabes, which sometimes requires years to attain its full development, since we can hardly expect that the quietly formed meningeal connective-tissue hyperplasia and the degenerative changes which follow it, can undergo perfect resolution. A favorable result can be looked for only when the infiltration is so slight as to be capable of being absorbed and when the degeneration is still of limited extent, the number of destroyed nerve elements being yet small. If now, in spite of these aggravating circumstances, we are sometimes able to obtain favorable results from the antisyphilitic treatment of tabes, the evidence thereby furnished of a causal connection of these cases with lues is so forcible that no reasonable doubt can be entertained. I will not deny that I formerly occupied an extremely reserved and even sceptical position on this question; and it was only after I had been forced to resort to antisyphilitic treatment, in a few cases, and was convinced of its excellent effect, that my conviction became stronger and stronger that the vast majority of cases of tabes are most clearly of a syphilitic nature. My first therapeutic attempt was made in the year 1886.

A married man 38 years of age, who had been infected with syphilis nineteen years previously and had had ulcerating nodes on the back and breast five years before, got a thorough wetting during a violent thunder storm two years before coming under observation. One year after this he began to suffer with severe "rheumatism," which was accompanied by difficulty in movement and weakness in the legs, especially on the right side, a feeling of tension in the back, and a sensation of constriction in the gastric region. The bowels were constipated, the urine was voided with difficulty. Of late the patient had complained of pain in the right arm, and movements of this extremity became uncertain. When I examined the man, undoubted symptoms of tabes were present (absence of patellar reflex, ataxia, etc.), together with thickening of both tibiæ and cicatrices on the back which had followed serpiginous ulcers; there were also disturbances of coördination in both hands, especially marked on the right side. In this case I was led to adopt an antisyphilitic treatment, on account of the periosteal thickenings of the tibiæ and the cicatrices of the back, which distinctly pointed to lues. I administered iodide

of potassium internally to the patient and gave subcutaneous injections of gray oil, which treatment was continued for four months with proper intervals. Improvement took place under my very eyes; the ataxia notably diminished, and almost entirely disappeared from the arms (the patient was a popular piano-teacher); the numb feeling in the legs also disappeared as well as the paræsthesia in the toes. The enemata which were formerly necessary to effect a movement of the bowels were gradually dispensed with, and at last became quite unnecessary. The urine was passed with much less difficulty.

In a few other cases in which the symptoms of tabes were associated with marked evidences of lues, the same treatment gave most gratifying results. This experience encouraged me to institute antisyphilitic treatment in other cases of tabes in which no visible signs of lues were present, and some of these also were very favorably influenced. Th. Rumpf, M. Benedikt, A. Strümpell, M. Dinkler, Renaud, and others have also occasionally obtained good results from the antisyphilitic treatment of tabes. After the experiences above mentioned, there remains no doubt whatever in my mind that a considerable number of cases of tabes have a direct connection with syphilis.

The weighty arguments derived from my therapeutical researches, from the anatomical findings, and from the statistics of large numbers of cases are convincing that to lues is to be assigned the most important rôle in the pathology of tabes. In spite of all this, however, we must admit the possibility that occasionally also other injurious influences (traumatisms, fatigue, excesses, toxic influences, etc.) may cause tabes, especially when they concur with syphilis, the main etiological factor.

As a matter of fact, tabetic symptoms, or at least such as are similar to those of tabes, may occur under other conditions. We have previously mentioned a few observations of disseminated nodules in the meninges, of a pronounced gummatous character, the symptoms of which were distinctly of a tabetic nature. Borgherini refers to a case of sarcomatosis of the spinal cord which had led to lesions of the posterior columns and nerve roots. It is also well known that diphtheritic paralysis, although occurring in acute form, occasionally imitates tabes; and also that ergotin poisoning excites changes in the spinal cord which have the greatest similarity, both clinically and anatomically, to tabes dorsalis (Fr. Tuczek). While admitting all this, we still must maintain that by far the most frequent cause of tabes is syphilis.

Symptoms.—In the multiplicity of the symptoms which are natural to tabes, a description which will fit all cases cannot be given, we will therefore confine ourselves to a recounting of the essential symptoms of the disease. Violent *pain*, which is described as tearing,

boring, fulminating, as though coming from the deeper parts, is the most constant morbid sign. It appears quite suddenly in paroxysms, disappearing again just as rapidly and sometimes for a long period (days or weeks); at other times, especially at the later periods, the painful paroxysms are of longer duration. These pains, which are frequently mistaken for rheumatism in the beginning, affect the lower extremities as a rule, but may also be troublesome in the testicle, bladder, and rectum, and attack the upper extremities, as well as the head (trigeminus area). Occasionally the pain is localized in a certain spot in the skin; in that case the latter is so hyperæsthetic that the slightest touch (pressure of the underclothes, etc.) becomes unbearable. Only in very rare instances does this hyperæsthesia extend over the whole body. Of frequent occurrence are various paræsthesias (feelings of numbness, formication, etc.) on the lower extremities and the trunk; quite frequently a sensation of cold in the legs and a girdle sensation of the trunk are present. On the arms the paræsthesia as a rule predominates in the area of the ulnar nerve.

Sensibility is frequently not disturbed; especially certain forms, such as tactile sensation and the temperature sense, do not show a marked diminution for a long period. In place of this there exists, however, localized analgesia, and the skin, especially of the lower extremities, is only slightly or not at all sensitive to the prick of a needle; or the sensation of pain is belated in reaching consciousness. In its further course, however, the sensibility becomes notably dulled over certain sharply defined cutaneous areas of greater or less extent.

Pain and paræsthesia as well as analgesia may also be observed in the trigeminus area (mucous membrane of the oral cavity); in rare cases the sense of taste is also affected. Occasionally trophic disturbances occur, during which the teeth become loose and fall out, and occasionally even small pieces of the jawbone are expelled. Among the early symptoms of tabes are also a diminution or loss of the patellar reflexes, and of the pupil reflex. These symptoms may, like all the symptoms of tabes, be unequal on the two sides, or marked only on one side. In some cases myosis is present, and paresis of the eye muscles is not of rare occurrence; this may be temporary at first and only later become permanent. So likewise atrophy of the optic nerves is occasionally observed early, and in time this leads to total blindness.

Disturbances of the bladder are rarely absent; as a rule evacuation of this viscus is difficult and slow. In the further course of the disease the desire to urinate is postponed, obviously for the reason

that the mucous membrane of the bladder perceives the fulness later than in health, and thereby the reflex contraction of the detrusor is delayed. Delay in evacuation of the bowels which is so frequently observed may be referred to similar causes. Occasionally impotence makes its appearance; in other cases it does not occur until very late.

A series of disturbances, known as "crises," are also important. Among these, painful attacks of vomiting, so-called gastric crises, belong to the more frequent symptoms, and sometimes appear very early. The individual attacks are only of short duration, but recur not infrequently at certain times, even in the early morning hours when the stomach is perfectly empty, or they continue for hours or days; suddenly the vomiting ceases and the stomach is again able to retain food. It is not without interest that some patients suffer from intestinal crises for a long time and very early in the course of the disease, so that thin slimy matter is evacuated perhaps for hours, and exceeding tenderness of the bowels is present, as is evident on the slighetest attempt at palpation.

Occasionally an accelerated action of the heart persists for a longer or shorter period. In rare cases the patient complains of a painful sensation, which radiates from the cardiac region to the shoulders—cardiac crises. Paroxysms of spasmodic cough accompanied by dyspnœa and a sensation of choking—laryngeal crises—are quite rare; more infrequently still occur the pharyngeal crises, described by H. Oppenheim, which consist of paroxysms of rapid movements of deglutition accompanied by a clucking sound. The most important symptom which, so to speak, impresses a signature on the disease, but which develops only later, is that of disturbances of the muscles. The muscles are not weak or paralyzed, but there is present a disturbance of coördination, *ataxia*. The legs are most frequently the seat of ataxia. The intended movements are carried out with over-expenditure of force, the patients throwing their legs forwards in walking, and bringing them to the ground with force. Even on a smooth road rapid turning is clumsy.

Ataxia is even more noticeable when the controlling influence of sight is absent, as is the case when the eyes are closed or in the dark. It is very characteristic of the disease that tabetic subjects begin to sway when the feet are closely placed together; this symptom sometimes even precedes the ataxia.

The upper extremities are also frequently affected by ataxia, when the clumsy use of the arms, hands, and fingers is noticeable. Ataxia of the facial and lingual muscles may produce disturbances of speech, but it is only rarely observed. Finally, various trophic disturbances of the skin, bones, or joints must be mentioned.

During the development of tabes the symptoms described are grouped together in different ways; in one case this, in another the other series of symptoms is prominent. In so far as tabetic subjects with extraordinary frequency have behind them a syphilitic history, it is certainly remarkable that the first symptoms of the disease make their appearance as a rule from five to fifteen years after infection, though sometimes earlier and sometimes later. In general, tabes begins during middle life; its course usually extends over ten or twenty years, and complications (frequently arising from cystitis or decubitus) finally bring on a fatal issue.

Not infrequently many disagreeable symptoms disappear and the affection remains stationary for years, so that the patient finds pleasure in working at his trade, and may even marry.

After the preceding explanations we think that we have solid grounds in the greater number of cases of tabes for assuming a preceding syphilitic infection. In some instances we are able to find unequivocal objective signs in the form of gummatous infiltrations and ulcerations or of perfectly characteristic cicatrices and pigmentations; more frequently still, a cicatricial remnant, a pigmented spot or one free from pigment may be demonstrated on the genitals, which betrays the infection. Very often the patient himself will give a faithful description, either of his own accord or when questioned, of his attack of syphilis. If the patient has no knowledge of any infection, and the objective symptoms just described are absent, occasionally important testimony can be elicited from the condition of his wife or children, or from a history of abortions which have occurred. Even when the examination gives only negative results, a previous syphilis cannot, therefore, with certainty be excluded. Leaving aside the evident fact that slight symptoms may have escaped the memory, there are some individuals who pay no attention to them. I have more than once encountered the most astounding negligence in patients who were undergoing treatment on account of diseases of the genitals with complications, and were consulting me from time to time, who appeared to be greatly astonished when their attention was called to a recent ulcerating infiltration of the penis, or to any other easily noted change. How slight a value should be set on the patient's previous history, Joseph Adolph Hirschl has recently shown. This observer took the trouble to look up the previous history of patients treated for marked gummata in my clinic in recent years, and found that in 36.5 per cent. no evidence whatever of infection or heredity could be found, in 9.5 per cent. infection could be assumed with probability, and in 54 per cent. with certainty. Therefore we cannot assert that even among those tabetic patients in whom the

most careful search does not reveal luetic antecedents, some may not have had syphilis of which they never became aware.

However, there may be a certain number of cases of tabes, although proportionately small, which are probably due to other injuries, as already mentioned; or these injuries may act in conjunction with lues.

The Peripheral Nerves.

Isolated syphilitic affections of the peripheral nerves are not frequently seen. Even though we must admit that manifold and often grave neuropathies occur during the various phases of syphilis, we do not yet know well their anatomical and histological changes.

Only in rare instances do nerves suffer compression by lymphatic nodules. In a certain number of cases gummatous infiltrations in the soft tissues, for example in the muscles and fasciæ, may press on nerve twigs, or the syphilitic products situated on the periosteum and bone, in depressions and on edges through and over which nerves take their course, exert pressure on the latter and thus produce neuralgias and paralyses. Or there are present gummata of the cerebral meninges which compress the nerves within the cranial cavity, as a rule in the neighborhood of the sella turcica, as has been found in the case of the olfactory, the optic, the nerves of the ocular muscles, and the trigeminus.

With our slight knowledge of peripheral nerve lesions, we must for the present leave undecided whether the seat of the disease for certain analgesias, which Alfred Fournier and L. Duncan Bulkley have observed in recent syphilis, should be looked for in the nerve centres or along the course of the nerves.

Neuralgia.

Neuralgic affections are quite frequently observed, and are not always confined to distinct tracts. Seeligmüller looks upon neuralgias which occupy an area on both sides of the skull in the form of a painful ring of about two or three fingers' breadth from the ear upwards (like a child's comb) as dependent on syphilis. I have observed neuralgias of a similar kind in early syphilis. Here, however, we are dealing with some of the symptoms of a meningeal irritation which has already been discussed. Neuralgias, however, may develop in the course of syphilis which follow very closely the course of certain nerves or nerve twigs, or which occur in an isolated manner in individual organs.

These affections of the peripheral nerves appear occasionally in

the early period of the constitutional disease or a few months later; at other times again years after the primary infection.

We have no knowledge whatever of the anatomical changes in the nerve affections occurring in the stage of irritation of lues, as there is no opportunity for their proper examination. The conditions are somewhat more favorable in the gummatous stage. Here we find gummatous infiltrations which have either extended from the neighborhood to the nerve substance and destroyed the latter, or have involved the neurilemma or the nerve itself in the form of a neuritis or perineuritis syphilitica, and destroyed it.

Neuralgic affections of the *trigeminus* are, on the whole, most frequently observed. The affection may occupy the area of distribution of any or of all the branches; occasionally it is confined to individual branches (supraorbital, lingual). I once had the opportunity to observe a neuralgia of the right supraorbital, in an old man thirty-one years after infection, which was caused by an enlargement of the upper margin of the orbit. Under antiluetic treatment the neuralgia disappeared, and the osseous enlargement was also diminished.

On the other hand, neuralgias of the *spinal nerves* are of more infrequent occurrence. In a few cases neuralgias have been observed in the neighborhood of the occipitalis major and the nervus auricularis magnus, which disappeared only after antisyphilitic treatment. The nerves of the brachial plexus are not often affected in the course of syphilis. In a case observed by me the neuralgia was caused by the pressure of lymph nodes on the plexus. In another case a female patient who complained of pain in the little and ring fingers of the left hand had, in addition to a gumma of the triceps and a subcutaneous gumma of the arm which was connected with the fascia, an infiltration of long spindle shape, corresponding to the left ulnar nerve. After the patient had been subjected to contitutional treatment and oleum cinereum had been injected locally, the infiltration became smaller, the pain in the little and ring fingers diminished, and only formication was left, which also disappeared after some time.

Now and then I have observed *intercostal neuralgia* in the irritative period of syphilis. Occasionally a syphilitic periostitis of the ribs is a causative factor here. *Sciatica* is frequently caused by syphilis. In one case I was able to feel the sciatic nerve behind the trochanter as a greatly thickened nodular band, which disappeared, together with the pain, after local injections of gray oil. In all probability syphilitic perineuritis was the condition present. Cases of an intractable sciatica in previously infected individuals, which finally succumbed to an antiluetic treatment, have been repeatedly observed.

Visceral neuralgias may probably, as a general rule, be referred to syphilitic affections of the internal organs (heart, coronary arteries, lymphatic glands, intestine, etc.), but the possibility of an individual syphilitic affection of the corresponding nerves must be admitted.

Paralysis.

Paralysis of motor nerves is more frequently met with. Certain *cerebral nerves* are here to be mentioned, among which the nerves of the ocular muscles are most frequently affected. As we have already mentioned, paralysis of the ocular muscles very often accompanies cerebral syphilis or even precedes it; peripheral paralysis, however, is also not at all infrequently found. It is characteristic of these, that they occasionally make their appearance suddenly in the same manner as monoplegias and hemiplegias, and disappear again just as rapidly, thus presenting a fugitive character.

Paralysis of the *oculomotor* is of most frequent occurrence. Very many, probably more than one-half of all forms of paralysis of this nerve, are based on syphilis. If the disturbance affects the oculomotor *in toto*, we find paralysis of the levator palpebræ superioris, of the upper, lower, and inner recti muscles, the obliquus inferior, the sphincter pupillæ, and the muscle of accommodation; and in consequence of this we find ptosis, double vision, and retardation of the eye in its motions downwards, upwards, and outwards, as well as dilatation of the pupil, which is neither contracted by light nor by efforts at accommodation. Occasionally the paralysis affects only single branches of the oculomotor. Quite frequently I have found the sphincter pupillæ paralyzed; at other times the paralysis affects the levator palpebræ superioris or one of the recti muscles of the eye; or indeed two or more branches at the same time. Quite frequently we find a paralysis of the abducens either alone or in conjunction with the paralysis of other ocular muscles, of which the trochlear is in general most rarely affected as a result of syphilis.

I have quite frequently found the *facial* nerve affected by paralysis in the course of syphilis, especially during the first year of the disease. In the majority of cases this paralysis also disappears altogether under constitutional treatment along with the other symptoms, and seldom are any traces of it left behind. This nerve, moreover, is also frequently subject to a rheumatic or other infectious paralysis —as Möbius would have us regard paralysis caused by "catching cold"; it may, therefore, easily happen that both injuries are present in facial paralysis. We find, at least, that a facial paralysis not very infrequently comes on in individuals who are or have been syphilitic,

after "catching cold." In recurrent facial paralysis, we should first of all think of syphilis, as also in cases of bilateral facial paralysis. The latter is of rare occurrence, and when present is to be referred to a basal cerebral syphilis, if there is also paralysis of other cerebral nerves, such as the auditory (W. R. Gowers), the oculomotor, abducens, trigeminus, auditory, and hypoglossal (J. Donath). The suspicion of a central cause should also be aroused if the paralysis is incomplete or involves only single branches. The peripheral paralysis is also characterized by non-irritability of the nerves and by muscular reaction of degeneration.

Peripheral paralysis of the other cerebral nerves is extraordinarily rare. Ernst Remak observed a paralysis of both accessory nerves and of both recurrent nerves. Peripheral paralysis of the hypoglossus also occurs, but rarely, while that of central origin is quite frequently encountered.

Should the affection attack mixed trunk nerves, both sensory and motor paralyses result. The disturbances caused here are by no means distributed equally; sometimes the sensory, at other times the motor are the most prominent. Thus, in cases of complete paralysis of the *trigeminus* the muscles of mastication, the masseter and the temporal, whose bellies can often be distinctly seen and always felt to contract in mastication, are found to be quite flaccid when the patient tries to close the jaws.

I have observed motor paralysis and sensory disturbances occurring in the upper extremities from a syphilitic tumor of the lymphatic glands. Similar observations have been reported by Léon Gros and Lancereaux, Th. Rumpf, and others.

Within the area of the sciatic nerves, which, as we have seen, are frequently to be affected under the picture of sciatica in syphilitic subjects, mixed forms of paralysis have been at times demonstrated; but here also pain is usually the most prominent of the nervous symptoms.

THE ORGANS OF SPECIAL SENSE.

The Eyes.

Among all the organs of special sense the eye is most frequently affected in syphilis, and more than that, it is one of the favorite localizations of lues. If we examine the outer protective parts, we find that the lids and eyebrows participate in all the forms of syphilitic lesions.

The initial lesion is rarely met with on the *eyebrows*. Ricord observed one such case, and in a case recorded by Morel-Lavallée an

initial lesion of the left eyebrow was caused by a bite during a scuffle. The constitutional syphilides here are of the same nature as those on other hairy parts.

Initial manifestations in the form of scleroses and papules have been repeatedly observed on the *lids* and at the inner canthus of the eye by myself and others. The modes of infection are various, and frequently cannot be discovered. Boucheron observed the initial lesion in a virgin following a kiss on the eye; Thiry saw it caused in a young man, who touched the eye with an infected finger; Hamande reports a case of chancre of the lid in an elderly man who became infected in a laundry where the linen used in a syphilitic ward was washed; Tepliaschin reports the case of a syphilitic female "healer," who was in the habit of licking the eyes of persons suffering with ophthalmia, and who in this way infected the lids of seven persons; in a case of Vose Solomon infection on the lid of a six-weeks-old child was received from a syphilitic aunt; and Snell relates a case of infection of the caruncle and the contiguous portions of the lid in the nurse of a syphilitic child. Desmarres reports a remarkable case in a physician who contracted an initial lesion of the lid by the saliva of a person suffering from syphilis of the mouth being thrown into his face during a coughing paroxysm. In one case I observed a typical initial lesion of the left lower eyelid together with one on the genitals in a young cadet; in a virgin I found ulcerating initial lesions on all four lids.

Although the syphilitic initial lesion probably runs the same course on the lid as elsewhere, it is, in fact, more unfavorable for the reason that, on account of the unusual situation, it is rarely recognized at once, and so is not properly treated. Ulceration and swelling of the surrounding skin, even chemosis of the conjunctiva and radiating pains accompany the affection, until proper treatment is instituted. In one case (Galezowski) a broad symblepharon was formed. The neighboring lymphatic glands, here the preauricular or submaxillary or both groups, are involved in the process, in the manner previously described.

Of the constitutional forms of syphilis, roseola macules, papules, and pustules are met with on the lids often as part of the symptoms of a neglected or malignant syphilide extending over the whole body; while gummatous infiltrations and ulcerations are associated with similar processes in neighboring parts (forehead, temple, cheek, nose), especially if they possess a serpiginous character, and they often destroy large portions of the lids. Most of these affections, however, may also, although rarely, occur alone.

The papules of the lids are generally covered by fatty scabs or

crusts, and being situated at the free border, like the pustules they have a tendency to become ulcerated. Loss of the eyelashes—*madarosis*—is in that case usually the result. Madarosis is, however, also observed without a previous affection of the lids, occurring independently or as part of the symptoms of a universal alopecia.

Gummata of the lids sometimes occur in the form of hordeola and chalazion, or they occur as flat, superficial infiltrations, or grow to tumors the size of an almond, a walnut, or even larger. At the same time the skin is usually affected, or the gummatous affection attacks by preference the cartilages—tarsitis syphilitica. The course is sometimes an acute one, but frequently it continues for several weeks; pain at times is quite severe, or again it may be entirely absent. Ulceration is quite common; the amount of disfiguration remaining behind after cicatrization will naturally depend on the degree of destruction. Infiltrations which do not go on to ulceration run a more favorable course as a rule, but they may also occasionally end in a loss of substance and subsequent contraction of the skin and cartilages. In proportion as the hair follicles suffer from the gummatous infiltration we shall also have a madarosis here.

On account of its unusual seat the initial lesion is at first sight frequently taken for a gumma; on the other hand, again, a thin gummatous infiltration may be mistaken for an initial lesion. Smaller syphilitic infiltrations of the lids might possibly simulate, in the early period, a benign chalazion or hordeolum. The differential diagnosis from *lupus Willani* or *lupus erythematodes* does not therefore offer any difficulty, because lupus attacks these portions as a rule only after the same affection has already made its appearance on the cheek or nose. We should, however, remember that in exceptional cases lupus may be confined to the lids, as I observed in one of my patients. It more frequently happens that a *cancerous* ulcer is mistaken for a syphilitic ulceration than vice versa. To avoid repetition the reader is referred to what has been previously said as regards all these conditions.

The various syphilitic affections are more infrequently met with on the *conjunctiva* than on the lids.

The initial manifestations (scleroses) are met with as a rule on the transition fold of the lower lid, more rarely on the conjunctiva tarsi or on the conjunctiva bulbi. Two cases are on record (Fournier, Michel) in which physicians treating patients affected with syphilis acquired a conjunctival chancre; once the affection was observed in a midwife (Desmarres, 1852), and this, we may observe in passing, is the oldest observation of the kind. In a case reported by Szokalsky a chancre of the conjunctiva in a child was caused in all

probability by an attempt made by a syphilitic to remove with the tongue an eyelash which had fallen into the conjunctival sac of the child. Conjunctivitis and photophobia frequently accompany the affection, which usually heals without any permanent injury, at the most a cicatrix being left. The preauricular or submaxillary glands become transformed into indolent buboes in the case of this lesion.

A stubborn conjunctival catarrh must occasionally be regarded as a symptom of constitutional syphilis. Hirschberg has also noted reddening of the conjunctiva in children with hereditary syphilis. Distinctly raised or only slightly elevated flat *papules* have been observed by me and others on the conjunctiva; these were accompanied partly with the same efflorescences of the general cutis or the lids, partly with other symptoms of syphilis.

The gummata of the conjunctiva generally extend to and involve the sclera, or they may involve the limbus corneæ if correspondingly situated.

I once saw on the right eye of a day laborer, 28 years of age, a rust-colored moderately hard infiltration the size of a pea, which mainly affected the conjunctiva, but also had its seat partly on the sclerotic; to the upper and inner side this infiltration touched a white corneal scar, which had been produced by a traumatism, and towards which the iris had been drawn and had become adherent; from below, a few larger twigs of blood-vessels were seen to pass to it. Both upper lids contained a number of tarsal gummata of the size of a small pea, which rendered the conjunctiva palpebrarum bulging, and on the free border of the right upper eyelid a small ulcer was seen. On the left side a retinitis was present. In addition to these lesions there were gummatous ulcerations in the pharynx and larynx, a few periostoses, and on the skin syphilitic pustules and deep gummata. Under a proper constitutional and local treatment all these lesions healed; both the conjunctiva and sclera became perfectly normal.

If the gummata go on to ulceration, a cicatrix or a pterygium-like thickening of the conjunctiva may be expected. In Wecker's case the conjunctival gumma was at first mistaken for a malignant neoplasm, until a further examination revealed symptoms of syphilis on the left arm.

The *caruncul*æ, which have already been mentioned in connection with the initial lesion on the lids, may also become the seat of gummatous infiltration. Because of the rarity of this affection the mistake was once made of taking this lesion for a cancerous ulcer, until R. W. Taylor effected a cure by antisyphlitic treatment.

We are in possession of only a few observations on syphilitic affections of the *lacrymal gland.* The *tear ducts* may become involved in morbid changes occurring in the neighborhood, either in the con-

junctiva and the lids, or on the mucous membrane of the nose. *Dacryocystitis* has been repeatedly observed by me in acquired as well as in hereditary lues. The lacrymal sac and duct are most intensely affected in ostitis and periostitis of the bony lacrymal canal. Since the work of Hutchinson, who looked upon a keratitis parenchymatosa in conjunction with a frequently observed deafness and anomaly of the incisors as an expression of hereditary syphilis (Hutchinson's triad), affections of the *cornea* are numbered among the most frequently occurring manifestations of syphilis. This same affection is referred by Horner to acquired syphilis. Mauthner once observed a stubborn keratitis parenchymatosa in an infant who had acquired syphilis from a nurse. We must, however, mention that tuberculosis may also cause a similar parenchymatous keratitis (E. von Hippel, Alexander). Aside from this, gummata of the cornea have been observed only in cases in which the infiltration extended to the latter from the neighborhood, and then in only a few cases.

The *sclerotic* is also rarely the seat of gummata. If gummata of the sclera are combined with other luetic affections of the eye or of other regions, they are early recognized as such; otherwise they may, on account of their rare occurrence, frequently be taken for malignant neoplasms, as in a case reported by Charles Higgins, in which finally appropriate medicinal treatment brought about a cure.

Syphilitic *iritis* is a disease of equal importance to the ophthalmologist and to the syphilologist; for, on the one hand, over one-half of all inflammatory affections of the iris are syphilitic, and on the other iritis is a very common affection, which is met with in all stages of lues, occasionally even as the first symptom of the constitutional affection. This is not the place to enter more minutely into the symptomatology and course of iritis (which belongs together with syphilitic choroiditis and retinitis to the domain of ophthalmology). It may, however, be said that this disease does not differ in most cases from the idiopathic form. Some authors (Stellwag, v. Carion, Edward v. Jaeger) deny, moreover, that there is any difference between syphilitic and idiopathic iritis. In a certain number of cases syphilitic iritis occurs with the formation of yellowish-red nodules, *papules* of the size of a pin's head, which according to E. Fuchs have their seat on the edge of the cilia or the pupil, but never between these two zones—*iritis papulosa*. In the latter course gummata are developed on the iris.

Although syphilitic iritis may heal spontaneously, we nevertheless must generally expect grave injury to the visual organ from the formation of posterior synechiæ or occlusion of the pupil. The inclination to relapses, the frequent occurrence of the same affection in

the other eye, the possible progress of the process to the ciliary bodies and to the choroid, and finally, though rarely, the formation of a secondary glaucoma, increase the danger of this affection greatly.

The *ciliary body* usually becomes affected secondarily to an iritis—*iridocyclitis*. Occasionally, according to E. Fuchs, we find gummata which have their seat in the iris as well as in the ciliary body, and may in the course of their growth even perforate the coverings of the eye, thus causing its destruction. Inflammation of the *chorvid* may in the same manner accompany iritis, but an independent syphilitic *choroiditis* may also occur. Diffuse exudative choroiditis is moreover frequently caused by syphilis; as also choroiditis centralis, in which the place of the macula is occupied by a copious exudation that later on changes into a bluish-gray mass of connective tissue (E. Fuchs). Choroiditis becomes dangerous when cloudiness of the crystalline lens occurs or if the retina or the optic nerve is involved. According to our present experience the syphilitic forms of choroiditis cannot be distinguished from the idiopathic forms (Mauthner). Affections of the *retina*, if we also include conditions of hyperæmia and irritation, seem to be of more frequent occurrence than has been assumed hitherto. Ole B. Bull has frequently observed hyperæmia of the optic nerve in early syphilis; the frequent appearance of retinal irritations has already been mentioned. More or less grave forms of marked retinitis are, however, also represented by a considerable fraction of the cases.

In affections of the intracranial portions of the optic nerve, or when gummata of the brain or its meninges are present, optic neuritis in its various forms may occur within the cranial cavity as well as in the course of similar non-syphilitic affections. Independent syphilitic optic neuritis, or neuroretinitis, has, however, also been observed. Retinal affections which depend on disease of the vessels of the retina are mentioned by Ostwald, Haab, Seggel, H. Magnus, and others.

In the course of cerebral syphilis *amblyopia* and *amaurosis* are of frequent occurrence, although the ophthalmoscope does not reveal the presence of any anomalies; at times the visual disturbance is only temporary.

Cloudiness of the *crystalline lens* caused by syphilis may usually be referred to an antecedent choroiditis, but it is possible that there may exist a *hyalitis syphilitica*.

According to Michel the crystalline lens may become diseased independently as a result of syphilis. Inasmuch as atheroma of the vessels leads to cataract, and as syphilis is the cause of such changes in the vessels, a connection between lues and cataract may be admis-

sible. In a case observed by Johann Scherl, a gummatous neoplasm of the iris and the ciliary body distended the lens; the anterior capsule of the lens was widely opened and the small-celled infiltration itself protruded between the fibres of the lens.

Syphilitic lesions of the *orbit* have already been discussed. O. Walter observed gummata in both orbital cavities in a three-and-one-half-year-old child. Occasionally the orbital gumma passes through the superior orbital fissure towards the median fossa of the skull.

The Ears.

Accounts as to the frequency of syphilitic ear affections are quite variable. According to James Hinton hereditary syphilis was the cause of more than one-twentieth of all ear diseases in Guy's Hospital. Albert H. Buck, of New York, was able to find but 30 cases due to syphilis among 3,976 cases of ear disease, but he believes that the percentage may be much higher, for the reason that the syphilitic origin of the ear trouble is so frequently unrecognized. A. Desprès observed among 1,200 syphilitic subjects papules on the external ear (and in 1 a venereal ulceration) in 5 cases; and Ravogli found the external ear affected in 1 case and the middle ear in 15, among 144 syphilitic patients.

Syphilitic initial lesions of the organ of hearing are very rare occurrences. Infection seemed to have occurred in one case through the use of a towel, in another by a kiss.

A number of years ago, a syphilitic infection by catheterization of the Eustachian tube, transmitted by a physician in Paris to at least five persons, aroused great excitement. Syphilitic infections caused in the same way have been but rarely observed since.

Irritative lesions of syphilis, such as maculæ, papulæ, pustulæ, and the forms of disease springing from them, such as scales, ulcerations, and cicatrices, are not very infrequently found on the external and internal surface of the concha of the ear, on the tragus, and on the external auditory meatus in patients who are also thickly covered on the rest of the body. As a rule we are then dealing with a greatly neglected case of syphilis. In exceptional cases we also meet with one or two papules in the external auditory canal where the skin syphilide is only moderately developed. I have observed complete occlusion of the external auditory meatus by a papule situated on the anterior wall, and with this was marked diminution of hearing. When the auditory canal is sufficiently wide, hearing is but slightly affected.

When the papulous infiltration is situated on the *drum membrane*

itself, it is another matter. In a female factory hand, twenty years old, suffering from syphilis, who complained of roaring in the right ear, I was unable to distinguish the different parts of the right membrana tympani. In the locality where the short process of the handle of the malleus was assumed to be, a pale, shining papule the size of a hemp seed was present; a few days later two ecchymoses were noticed in the right membrana tympani. Recovery speedily took place. As long as only the external part of the ear, including the meatus auditorius and the external layer of the membrana tympani, is involved a permanent loss of hearing is not ordinarily to be feared. The course of ulcerated papules is also favorable, even when they lead to flat or depressed cicatrices in the auditory canal, accompanied as a rule by a falling of the little hairs (Adam Politzer).

Gummatous ulcerations of the auricle have been observed by me, although they are not often found on the external ear. Diffuse gummatous infiltrations lead to atrophy and contraction of the cartilages of the ear. I have also seen gummatous ulcerations in the external auditory canal. In rare instances a circular contraction will be formed here (Tröltsch).

Affections of the *middle ear* usually accompany a syphilitic pharyngitis and rhinitis; contraction or occlusion of the tube at the ostium pharyngeum by syphilitic papules or gummatous nodules (Zaufal) will be accompanied by temporary shrinking and contraction during cicatrization with permanent loss of hearing. The otitis media in which the inflammation is transmitted through the tube, as well as that which occurs independently in the course of syphilis, is accompanied by purulent inflammation and cloudiness of the membrana tympani, occasionally by its perforation (H. Knapp), frequently without pain and with ringing in the ears. The bone conduction in complicating disease of the labyrinth is lowered and a restitutio ad integrum is in this case rarely to be expected. Following syphilitic affections we may have caries and necrosis of the tympanic cavity and also of the mastoid process and petrous portion of the temporal bone, occasionally with a fatal result (Politzer). Affections of the *auditory nerve* and of the *labyrinth* (the *cochlea*) are very rarely observed during the period following shortly after infection. In the great majority of cases, however, syphilitic affections of the internal ear manifest themselves after the infection has already existed for a long time, and lead to either sudden or gradually developing deafness. In a few cases temporary improvement is seen, but as a rule permanent loss of hearing results.

According to J. Gruber, a labyrinthine affection occasionally appears in syphilitic patients, either as the result of catching cold or

without any discoverable cause, which suddenly and permanently destroys the power of hearing. Bone conduction is diminished in this case, and the perception of high tones especially is lowered. The otitis interna is furthermore troublesome by causing noises in the ears, attacks of vertigo, and disturbances of equilibrium. The affection exists usually on both sides, and one ear generally seems more affected than the other.

Occasionally disturbances of the function of hearing constitute one of the symptoms of cerebral syphilis, especially of basilar meningitis; as a rule there is also present in this case a paresis of other cerebral nerves. In one case I noted the occurrence of deafness soon after the appearance of constitutional symptoms; accompanying a nodular syphilide which showed some tendency to break down, there existed a weak memory, diabetes insipidus, and a lowered hearing power on one side, which would at times sink to absolute deafness. The disturbance may also manifest itself in the form of hallucinations of hearing (James B. Ayer).

According to the nature of the case syphilitic affections of the external ear admit of a more favorable prognosis than those of the middle ear, while the labyrinthine affections afford the worst prognosis. The syphilitic processes of the external ear are, however, now and then complicated with those of the middle ear and the latter again quite frequently with labyrinthine syphilis. Occasionally the disturbance of hearing is caused by a central affection. These conditions must therefore be carefully considered in making the diagnosis and prognosis.

The Organ of Smell.

In discussing rhinitis syphilitica we have already mentioned manifold changes in the sense of smell. There seems to be no doubt, also, that in the course of many cases of cerebral lues the *sense of smell* is disturbed or totally abolished. Thus we find an observation recorded by Fr. Chvostek of a case of cerebral syphilis in which besides other symptoms dulness of hearing and of the sense of smell was present. Naturally, however, the examination to determine this point is usually impossible on account of the accompanying loss of intelligence or even of consciousness. The case is different if a syphilitic affection of the olfactory nerve is present, and the intellect is not at all or not continuously clouded. In this relation a communication by Westphal is interesting. According to him, the convulsions of a syphilitic subject usually made themselves known some time before by an "hallucination of smell." This consisted in an odor which the patient compared at times to spirit of ammonia, but which

was usually designated by him, with an expression and features of intense disgust, "a cadaver-like odor." The record of the autopsy, among other things, says that both olfactory nerves were very long, the bulb was flattened, and the right one in its middle portion was somewhat strongly adherent; beside this adhesion two gummatous nodules somewhat larger in size than the head of a pin were situated prominently within the pia. In addition to basilar meningitis there is occasionally present some impairment of the sense of smell, as a result of the involvement also of the olfactory nerves.

The Organ of Taste.

The taste may also suffer from the frequently present syphilitic processes on the tongue (and on the palate), especially as regards the finer distinctions. Disturbances of this centre from affections of the central or the peripheral tracts are but little known. Richard Hitschmann has described a lowered sense of taste and smell occurring in a syphilitic subject.

We should understand, however, that syphilitic affections may involve the glossopharyngeal or the fibres of the chorda, and cause gustatory alterations. Piogey observed a loss of taste in a man suffering from a neuralgia of the third branch of the trigeminus who had been infected twenty years previously. Iodide of potassium brought about a cure.

ABNORMAL COURSE OF SYPHILIS.

Now that we have concluded the description of the syphilitic process in all the organs and tissues, it will probably be easy for every one to bear in mind the picture of a syphilitic affection and to follow its course. We must, however, repeat again and again, that syphilis does not follow the same course in every individual. At times only portions of the skin, the mucous membrane, the subcutaneous or submucous tissue, the muscles and fascia, the bones, cartilages, and joints, the nervous system, the intestines, glands, etc., become affected independently and in isolated form; at other times we find the different organs affected in varying proportions; at still other times the morbid process attacks extensive portions of one or the other tissues—occasionally with an especial predilection for one half of the body—while at the same time other kinds of tissue are affected only in a subordinate manner, or not at all.

As regards relapses, there is no law so far as our present knowledge goes. Long intervals of time are recorded in the great majority

of observations during which lues does not disclose its presence by a single symptom (being therefore *latent*). I am disposed to maintain, in the light of unbiassed experience, that in the majority of cases perfect recovery from lues occurs with the subsidence of the irritative forms. In only a very small proportion of cases of syphilis does a portion of the virus remain dormant for some time and cause the development of morbid products in more or less important parts after the lapse of years.

But there are also individual exceptions to be recorded in which syphilis, as we have pointed out previously, presents a totally different picture, in that new attacks occur in rapid succession, and occasionally in such severely dangerous forms as to constitute entirely atypical forms, the so-called syphilis acuta, præcox, and maligna. Something similar is observed in "spedalskhed." This is, as a rule, "a chronic disease, but in some rare cases we observe that it runs a very rapid course; it reaches a point of development in months, for which years are otherwise necessary" (W. Boeck).

To avoid a confusion of ideas, we should do well to differentiate syphilis "præcox" and "maligna" from syphilis "gravis." Thus, a case of syphilis, the gravity of which is due solely to the localization of syphilitic products in functional and vital organs, deserves the name of syphilis "gravis," but it should not be classed with the malignant forms of lues.

On the other hand, we not infrequently have opportunity, when we have access to a large clinical material, to observe the occurrence of later forms (subcutaneous, periosteal, gummata, and others) at the same time with the first general eruption. This occurrence, which in itself is not so unusual, by no means justifies us in speaking of a special variety of lues. When, however, the gummatous deposits in early periods of syphilis are markedly conspicuous as regards both their number and their rapid course, it is certainly proper to express this character of the disease by the term syphilis "præcox," or "acuta." In syphilis "maligna" a tendency to ulceration and necrosis of the syphilitic products is also added to the acute course. We must, however, admit, that the border line between syphilis præcox and maligna may also disappear, or rather that syphilis præcox occasionally passes into syphilis maligna.

The malignancy of syphilis is mostly shown by the fact that grave general disturbances (discomfort, pain in the limbs and head, fever) make their appearance after the initial lesion has existed for but a short time, and are soon followed by a copious eruption of polymorphous cutaneous lesions. In other cases the so-called prodromal symptoms cease with the appearance of the syphilide, or at least a

few days later, but the grave general symptoms (fever, pain, etc.) continue and greatly debilitate the patient. In addition to this, most of the roseola spots as rapidly change into pustules as the papules do into ulcers. We are then dealing with a pustular and papulopustular syphilide, which is rendered still more grave by the fact that added germs (usually staphylococci) cause the production of phlegmonous areolæ and irregular zones of inflammation around the efflorescences, and so help to maintain the fever.

In other cases the general symptoms are at once ushered in with cutaneous and subcutaneous nodules, the greater number of which rapidly break down or become gangrenous.

Extensive ulceration caused by increasing disintegration or mortification is characteristic of malignant (galloping) syphilis. In this case we also meet occasionally with hemorrhages, which may in part be due to luetic disease of the blood-vessels, in part to a changed condition of the blood. This form of lues is also characterized by the fact that the morbid products do not become aggregated into groups and that the ulcers do not take on a serpiginous aspect.

While the phenomena so far described may very well be explained by the acuity of the process, it is difficult to comprehend why in these cases the mucous membranes, but especially that of the oral cavity, are very rarely involved. In exceptional cases only the syphilitic products become localized within the nasal cavity, where they also break down rapidly, often resulting in necrosis of the bones and cartilages. More commonly there are developed rapidly disintegrating infiltrations and tumors in the muscles and bones or grave complications on the part of the organs of special sense (iritis, retinochoroiditis) and of the nervous system.

The cause of the malignancy has not yet been sufficiently explained. It is quite possible that we have here to do with an increased virulence of the specific contagium. Certainly in the heredity of syphilis the difference in the virulence, at least as regards its diminution, may be instructively demonstrated clinically. On the other hand, we can conceive that individuals in whose ancestry there was never any taint of syphilis might be more gravely affected by the virus on account of their negative immunization; the syphilitic virus would in such a case possess an increased virulence only in relation to the host. After having once discovered the nature of the virus, we may hope also in this regard to learn more of its varying degrees of activity. I do not believe, however, judging from clinical observation, that an increased virulence of the contagium is the cause of malignancy. The form and appearance of the initial lesion are certainly not decisive here; for it is a common ex-

perience that the gravity of the future symptoms is altogether independent of the condition of the initial lesion. True, we not infrequently find a phagedena of the initial lesion in malignant syphilis, but it seems to me more correct to look upon this as in itself an expression of a bad constitutional condition. And, indeed, nearly all individuals suffering from malignant syphilis, as a matter of fact, present a marked depravation, such as scrofula or tuberculosis, or still more frequently alcoholism, malaria, scorbutus, or some other grave affection which has debilitated the organism previous to infection; or some debilitating factor of a temporary nature, such as loss of blood, pregnancy, or nursing, has rendered the organism less resistant to the action of the specific virus. For the same individuals who find difficulty in becoming acclimated in a strange land, especially in the tropics, or who have been greatly reduced by the diseases endemic in hot countries (such as anæmia, affections of the liver, dysentery, yellow fever, etc.), suffer more severely than others from a syphilitic infection, as the disease usually attacks them in an altogether peculiar, turbulent manner, and assumes a very grave form. According to my experience, the European in the tropics has nothing greater to fear than a syphilis which may be acquired there.

The syphilitic process may undoubtedly also be aggravated in a perfectly healthy individual by the intercurrence of injurious influences of any kind. As regards the influence of traumatic, chemical, or other injuries on the syphilitic, the following reflections suggest themselves: The injury alone cannot possibly produce a syphilitic lesion, but the intervention of the virus (or one of its derivatives) is always necessary. During the time that the virus circulates in the blood, most localities answer such an insult by the formation of a syphilitic lesion. In the latent period, on the other hand, an irritation (a wound or the like) may be expected to produce a syphilitic infiltration only in those localities where some portion of virus is present in a quiescent condition. Nevertheless it is possible that the virus may have been carried from some other part to the seat of the injury while the effects of the latter were still present. I am in hopes that we are not very far from the time when we shall be able to demonstrate the virus of syphilis in an indubitable manner in any locality in which it may be, so that we shall here find the explanation we desire. In the mean time, however, we may note the discovery made by Neumann that the microscope will reveal traces of infiltration from four to eight months after the seemingly perfect involution of a syphilitic eruption. In all probability a trace of virus is also left behind in some of these cases, and this will be aroused to renewed activity in the propagation and formation of

syphilitic lesions by the fresh irritation. We can also thus conceive why the "cauterisatio provocatoria," recommended by B. Tarnowsky, though occasionally provoking syphilitic lesions, also fails in many instances to do so.

We will now turn our attention to the facts gained by clinical experience concerning the influence of other morbid conditions on the syphilitic process, and vice versa.

The combination of syphilis with vaccination has already been referred to; the combination of the syphilitic virus with the venereal ulcer has also been mentioned. As regards the latter we may also state that the belief held by many, that constitutional syphilis more rarely occurs in cases of the contemporaneous development of a venereal ulcer, may have its foundation in the fact that the syphilitic virus is occasionally entirely destroyed by a symbiosis with the virus of the venereal sore—perhaps on account of the more rapid growth of the latter. The aggravating effect which the added pus cocci exert on the syphilitic lesions has also been previously touched upon.

The behavior of constitutional syphilis upon the intercurrence of some *acute* general affection is very remarkable. We have already discussed this question to some extent, and will only repeat that syphilitic lesions as a rule disappear in the course of febrile processes; and this is especially marked in the case of erysipelas, according to my experience. As a rule, however, the syphilide reappears several weeks later. In exceptional cases syphilis is said to have been permanently cured by such intercurrent affections. Something similar has been occasionally observed also after pneumonia, typhoid fever, etc. That experiences just the opposite of this have been recorded does not alter the fact. Thus, occasionally, such an intercurrence produces the opposite effect; the intercurrence of measles may aggravate the preëxisting syphilis, and smallpox also may exert an unfavorable influence on lues.

Chronic affections which in themselves exert an injurious effect on the organism are frequently made worse by the addition of syphilis; and, on the other hand, the syphilitic process may likewise become worse in such a case, distinguishing itself by a stubborn course; this is particularly true in the case of scrofula and tuberculosis. These affections may, however, also be directly excited by constitutional syphilis, when a predisposition to them is present. Complications of syphilis with lupus and cutaneous tuberculosis I have frequently observed. According to Verneuil, a syphilitic stricture of the rectum is usually complicated by pulmonary tuberculosis. Other affections (especially those of the skin), so long as they do not influence deeply the general constitution, are as a rule not at all or only very little

affected by syphilis; they also alter the syphilitic process but rarely as a rule. Here and there I have observed a *toxic* exanthem (drug eruptions and the like) in the luetic subject. So long as the lesions present an acute character they are easily recognized; but if they continue for a longer period, which is sometimes the case, leading to infiltration and pigment deposits, they are not always easily differentiated from cutaneous syphilis. An exudative erythema following antipyrin, salol, and other drugs, occasionally leaves deep pigmentations which last a long time. A bromide eruption frequently suggests, by the peculiar grouping of its lesions, the recurrent papular syphilide. Erythema multiforme, eczema, prurigo, and psoriasis deserve mention in connection with syphilis only in so far as their presence may, under certain conditions, increase the difficulty of the diagnosis. We may note that in individual cases the plaques of psoriasis are thicker in syphilitic individuals, present more infiltration, and have a darker color. This will be seen, however, as seldom as the case observed by Bulkley, in which syphilitic nodules developed on an eczematous ground. When syphilis and scabies were combined, I have not infrequently observed the transformation of the excoriations from scratching and the itch lesions into syphilitic infiltrations.

The syphilitic process may, on the whole, be influenced by the most diverse physiological and pathological conditions. Syphilitic infiltrations and ulcerations situated in unfavorable localities, for example on the leg, are occasionally distinguished by a course as stubborn as that of non-specific ulcers in these parts. A similar effect is produced by circulatory disturbances occurring in pregnancy. Thus congestions of the genital region in the pregnant woman are proved to cause a much greater distinctness of the syphilitic lesions (initial manifestation, mucous patches), which, however, fades out as a rule quite rapidly after confinement. According to Mewis, however, the lying-in woman suffering from recent syphilitic lesions of the genitals is predisposed to parametric exudations. Dystocia due to syphilis has already been spoken of.

The idea that *wounds* in syphilitic subjects cause most unfavorable complications is nearly as old as the medical history of syphilis itself; but opposition to such a view appeared equally as early, and it was maintained that wounds healed normally in the syphilitic subject. The general use of mercury has, moreover, complicated this question, for retardation in the healing of such wounds has from time immemorial been attributed by some to the action of the mercury rather than to that of the disease.

In several parts of this article we have emphasized the fact that

traumatisms resulting from outside influences occurring in the syphilitic subject, can cause the appearance of a syphilitic lesion at the place of the injury. It is remarkable, however, that slight irritations of longer or shorter duration should produce such effects earlier than grave lesions caused by momentary force (incised wounds, fractures, etc.). Thus a fly bite may be transformed into a stubborn syphilitic ulcer. As already mentioned, I have seen the eruption of scabies take on a syphilitic character. Alexander Gay observed the development of seven syphilitic papules from the same number of leech bites.

I have observed the abrasions produced by scratching in syphilitic subjects gradually transformed into luetic infiltrations and ulcers, the origin of which could for a long time be recognized by their form and direction. Appearances similar to these become more rare, however, the longer the time since infection occurred.

We must, furthermore, remember that when a traumatism is inflicted on the seat of a syphilitic infiltration or in its neighborhood the process will the more certainly invade the injured part the less the syphilitic lesion had progressed towards involution.

The wound of a tracheotomy performed on account of laryngeal syphilis or the parts of the trachea pressed upon by the cannula may also become the seat of a syphilitic process. Surgical practice has also furnished us with experiences of this kind in lues of the bones; for example, a bullet wound causing fracture of the bones of the leg, in an individual affected with a syphilitic hyperostosis of the tibia, has been observed to take an unusually long time to heal (Langenbeck).

Profuse, even fatal hemorrhages, as well as smaller bleedings, occurring either spontaneously or after slight operations in syphilitics, find a natural explanation in the fragility of the vessels caused by syphilitic arteritis or in a complication with hæmophilia, or they may be looked upon as the expression of a septic infection. In rare cases, however, the hemorrhagic diathesis may be directly caused by syphilis, or at least a latent predisposition may have been awakened by the latter. Injuries of the soft parts and of the bones caused by sharp instruments, bullets, etc., will in most cases heal without any trouble, and only rarely will delay be caused by various circumstances (fatigue, privation, dyscrasiæ) or occasionally by the formation of a syphilitic lesion. We are in possession, as a matter of fact, of numerous observations of amputations and other capital operations undertaken in the syphilitic which healed without any complications.

My own experience in this direction has also been very favorable.

I have frequently undertaken operative procedures in the syphilitic, and only rarely have had any bad results. I have even found in some cases that syphilitic lesions which had for years resisted the usual constitutional and local measures were cured promptly by a purely operative procedure. Thus, in the case of a puella publica who had been repeatedly and unsuccessfully treated in syphilitic clinics (in my own included) for an ulcerating gumma of the size of an apple on the left vaginal wall, I extirpated the ulcer and its surrounding infiltration and obtained healing by first intention, and, as I was able to demonstrate later, with a permanent result. An intelligent man, a mechanic, who had gummatous ulcers in the right groin, attended numerous clinics in Germany without being cured. I determined to extirpate the ulcers, and to graft according to Thiersch's method on the denuded portion, which was 7 cm. long by 4 cm. broad. In spite of unfavorable local conditions (it became necessary to incise an abscess of the lymphatic glands, and the dressing had to be frequently changed on account of the copious suppuration), a perfect cure resulted. When, after many months, I again saw the patient, the cicatrix was in excellent condition and nowhere was there any infiltration or inclination to disintegration. The result in a puella publica, twenty-six years of age, who had suffered so much from recurrent syphilitic lesions that she made an attempt at suicide to escape the torture, was very striking. In this condition of mind the patient entered my clinic. Numerous cicatrices present on the body testified to a grave lues, from which the patient had suffered for two years. In spite of varied antiluetic treatment in different special clinics, new gummatous foci had made their appearance, and had involved the skin, subcutaneous tissue, and muscles of the left calf. Besides this there were present broken-down gummata of the flexor surface of the left knee, where the skin was raised for a distance of about 6 cm. towards the thigh by a softened gummatous infiltration. I extirpated the gumma on the left calf, removing skin, subcutaneous tissue, and muscles as far as they were diseased, waited until healthy granulations had sprung up, and after scraping off the latter covered the wound, which was 10 cm. long, of equal breadth, and 2 cm. deep, involving also the muscular tissue by a plastic operation according to Thiersch. I scooped out the gumma in the bend of the knee as well as the gummatous cavity of the thigh, made a counter-opening in the upper end of the cavity, and put in drainage tubes; healing followed in a short time everywhere. In this case also the process would certainly never have healed without a surgical operation. The fact that the patient visited my clinic one year later, on account of gummata of the forehead and after another year for an ostitis gum-

mosa of the nasal bones, enabled me to observe with satisfaction that the field of the Thiersch plastic operation, as well as the other parts operated on, remained perfectly healed and did not present any morbid changes whatever, although the lues, as was proved by the affections of the forehead and nose which appeared later, had not as yet been eradicated.

Even when I have been obliged to operate within the area of a syphilitic infiltration I have been able to induce a favorable course of the wound where it was possible to operate aseptically or antiseptically. Gangrenous forms of chancre within the prepuce which had caused inflammatory phimosis and septic fever through obstruction to the escape of the discharges have been operated on by me without much fear. After scooping out and cauterizing the gangrenous ulcers under careful antiseptic precautions, I have sutured the edges, and usually obtained a cure by first intention. In such a case it is of course possible that the cicatrix may become the seat of an induration, owing to an overlooking of a portion of the original infiltration, the result being similar to what we see after an incomplete excision of an initial sore.

Tuberculous and Cancerous Transformation of Syphilitic Lesions.

Syphilis may by its manifold histological changes, perhaps also by the action of the toxins derived from the specific contagium, cause such essential alterations that the organism is thereby weakened and more readily attacked by other, partly functional, partly organic affections. That long-standing cutaneous syphilitic infiltrations finally take on, as a rule, the appearance of lupus was demonstrated by me many years ago. In these cases the lesion obviously offers a favorable place of settlement for tubercle bacilli. Sasakawa, a pupil of Neisser, has succeeded in demonstrating the presence of tubercle bacilli in such cases. If this occurs in the skin, the assumption is certainly justified that similar changes may also occasionally take place in neighboring organs.

Syphilis has also been held responsible by many authorities for the occurrence of various neoplasms. We are, however, still ignorant of the relations which neoplasms bear to syphilis, and all we can say is that cancers occurring in syphilitic subjects are for the present to be looked upon as ordinary complications. I regard in the same light the coincidence of ordinary nasal polypi and gummatous rhinitis, an instance of which I once met at my clinic in the person of a woman thirty-six years of age.

The case is different when the neoplasms are developed in places which have formerly been the seat of syphilitic lesions. We not infrequently observe that cicatrices following syphilitic ulcerations may become hypertrophied and assume a keloid-like appearance. In time, however, especially if a proper general and local treatment has been carried out, these cicatrices lose their bulky character and may even become very soft. Observations to the contrary have, however, also been recorded. Thus Samuel Wilks observed the development of a keloid in a cachectic syphilitic individual on the soil of ecthyma pustules, which were still enlarging and multiplying at the end of two years. That the opaque plaques of the tongue or the mucous membrane in general, which occasionally remain behind in syphilis (leucoplakia) may develop into carcinoma has already been metioned. In such cases, the enormous epithelial hyperplasia is changed into characteristic cancerous new growth. There is nothing specific about this, however, and the change is to be explained in the same manner as the development of carcinoma from a wart.

I and others have repeatedly observed cases in which syphilitic infiltrations have become converted into malignant neoplasms. These occurrences are analogous to those in which conditions of infiltration of long standing, whatever their character may be, have finally led to cancer.

Syphilitic Cachexia.

That the syphilitic process by its localization in organs and tissues of a higher physiological dignity exerts a pernicious retrograde action on nutrition and other important functions, we have repeatedly had occasion to point out. Symptoms will thus be produced which represent what we designate as syphilitic marasmus, or syphilitic cachexia. With these we must also class syphilitic anæmia (see above).

Amyloid Degeneration.

Amyloid degeneration is of very great importance. According to Virchow, Rayer was the first to recognize the direct relationship of this degeneration to syphilitic cachexia. Further researches have shown that amyloid degeneration is developed just as frequently, if not more so, as a result of hereditary syphilis as after acquired syphilis; Rokitansky even found congenital amyloid degeneration of the liver in children of syphilitic parents. Although Cohnheim found amyloid degeneration of the spleen and kidneys in the suppuration of bones following bullet wounds, some months after the injury, it nevertheless seems to me that this degeneration follows

most frequently a long-standing syphilitic process; when once originated, however, it continues even after the latter has long since undergone involution. Chronic tuberculosis is next after syphilis and chronic suppurative processes of the bones and joints (occasionally also of the soft parts) in the frequency with which it is accompanied by amyloid degeneration.

The vessels, and with especial frequency the small arteries and capillaries, more rarely the veins, are primarily attacked by this form of degeneration. In cases in which the disease is extensive, the small vessels of nearly all the organs are found to be degenerated. Even in a less extensive degeneration, however, a contemporaneous affection of the spleen, the liver, and the kidneys, and frequently also of the intestinal canal, is quite commonly encountered.

The liver in this case appears enlarged (preceding syphilitic processes may, however, have caused a diminution in the size of the organ), firm, and gives a feeling of fulness and pressure; icterus rarely occurs. If ascites is present, it is to be referred to the hydræmia accompanying amyloid degeneration. The symptoms of amyloid degeneration of other organs (spleen, kidneys, intestinal canal) are also present, and they will prevent us from mistaking the condition for a fatty liver.

An amyloid degeneration of the spleen is probably most frequently caused by syphilis. The organ is enlarged, and the condition declares itself subjectively by a feeling of fulness.

In amyloid degeneration of the kidneys the urine, although variable in amount, is, as a rule, copious and frequently contains a large percentage of albumin. The urine is otherwise clear and limpid; its specific gravity is very low or very high, according to the quantity; casts are only rarely found, and in any case are few in number. Œdema of the lower extremities and ascites are frequently observed and are due to the hydræmic condition of the blood. Uræmic symptoms are developed in rare cases only. Symptoms of cardiac hypertrophy (which are present in contracted kidney) are absent.

If amyloid degeneration of the intestinal mucous membrane is present, the patient will also suffer from anorexia, periodical vomiting, and pale, slimy discharges from the bowels.

Some authorities believe in the possibility of a cure in degenerations of a slight degree, but the most frequent course is that, after amyloid degeneration is once established, it invades larger and larger territories and of necessity results in death from anæmia and other grave disturbances of metabolism.

Although syphilis, as we have repeatedly had occasion to remark, results in a cure in the great majority of cases, it must be regarded

as one of the most serious diseases, on account of its great prevalence, and also on account of its injurious action on the functions of vital organs, as well as from the fact that it leads to many other grave affections. When we also consider the great havoc which this disease produces in the progeny, lues must be looked upon as one of the most dangerous of human affections, which may lead to the most dreadful results, and even to the depopulation of whole areas, if proper attention is not directed to it.

TREATMENT.

In entering on a discussion of the treatment of syphilis, I wish to emphasize the belief that the virus which has entered the organism may also die out spontaneously, that syphilis may therefore be cured occasionally without the intervention of drugs. When this spontaneous recovery takes place the disease usually comes to an end with the appearance of a few products of an irritative character. William Ferguson observed this among the native population while he was on duty with the British troops in Portugal, and he asserted that syphilis runs a milder course among this people. On account of the possible occurrence of a spontaneous cure, some have left syphilis to its natural development and have thus reduced treatment to a very simple regimen, the "simple treatment." The value of the statistics of this method is undoubtedly greatly depreciated by the fact that many non-syphilitic venereal affections have been included. Furthermore, many even of the advocates of the "simple treatment" have been forced to return to mercury, because they found that syphilis by no means always runs its course benignly.

Although, as already remarked, I am convinced that lues in the great majority of cases runs a comparatively mild course, we are nevertheless not justified in a policy of inaction, for the simple reason that in any individual case we have no data upon which to base a positive prognosis of the further course of the disease. On the other hand, it must be honestly admitted that while we can, probably in the great majority of cases, not only cause the disappearance of the symptoms but also prevent the transmission of the disease by heredity, yet up to the present time we do not possess any mode of treatment by which we can positively cure this dangerous disease radically and thus absolutely protect the patient against relapses. As a comforting fact, however, we may repeat that, by the rational use of the curative means which we already possess, we are able in numberless cases to effect a perfect cure of syphilis; and the proof of this statement we find in the freedom from further symptoms of the pa-

tient himself, as well as the escape of his progeny, and especially in the fact of occasional reinfection. In the following pages my task will be to present the method which has given curative results in the shortest possible time.

At the beginning of this work we expressed a belief in the organic nature of the syphilitic virus. Much research is being constantly conducted with the object of solving the mystery of the syphilitic contagium, but the practical physician must await results, and for the present take into account only those products of the specific contagium which clinical experience and pathologico-anatomical research have revealed to us. We can as yet only surmise what changes are to be referred to the action of the metabolic products of the syphilitic virus, and for this reason we shall for the present have to consider mainly the formative irritations which are caused by the virus.

We may assert that, with very few exceptions (in which examination, in all probability from the insufficiency of our methods, has given no results), every affection caused by syphilis is accompanied by demonstrable anatomical changes. We have every reason to believe that the disease products are caused by the colonization of the specific contagium which has entered into the body from without, and in its further course reached the tissues through the lymph and blood circulations. Our endeavor must, therefore, be to render the virus innocuous in all those places where it makes its presence known by exciting morbid changes, or at least to weaken its effects as much as possible.

From this it is evident that we lay the greatest stress on the *local treatment* of the syphilitic products. It must be admitted at the outset, however, that it is not always in our power to treat at once the disease focus, either because (on account of its seat) it cannot be reached or because of some other impediment. In these cases we must endeavor to apply efficient reparative measures as near as possible to the seat of the local lesion, that is to say, to institute *regional treatment.* We are obliged, moreover, to make use of remedies which affect the body *in toto,* that is to say, we introduce our remedies into the fluids circulating all over the body, and thus institute *general treatment.* When we introduce remedies into the organism, in the manner which will be described later, the possibility is at all events present that they will reach the disease focus by the same path (namely, that of the blood circulation or lymph current) by which the virus has entered. According to the nature of each special case the local, regional, or constitutional treatment is employed either alone or in combination with other measures. Most syphilitic products undergo a marked involution under the influence of certain drugs;

and these latter have, therefore, been praised as "specifics" from time immemorial. So far as local treatment is concerned, their effect is mainly to be referred to the fact that they are destructive to the virus. In the case of general or constitutional treatment we must, however, also admit that the so-called specifics do not effect a cure solely because they finally reach the diseased focus, but also through the favorable influence which they exert on the diseased organism *in toto*. The *modus operandi* of this is, we are forced to admit, as yet unknown to us.

Hygienic Treatment.

The most important factor in causing the involution of the pathological products must be assigned under all circumstances to a rational mode of life of the patient. This affords a ready explanation why at times very small quantities of the remedy (mercury or iodine) effect a marked involution of the disease, while frequently the largest doses remain absolutely inert in cases in which the patient lives an irregular life. The result of each of the methods of treatment mentioned or of any methods whatever may, as a matter of fact, be most uncertain if the patient does not live up to the laws dictated by sound reason. I have repeatedly observed that syphilitics (those recently infected as well as those with constitutional symptoms) who do not leave their arduous vocation while under treatment, or who, on account of duties imposed by society, continue in the same round of dissipation as before, but are otherwise treated *secundum artem*, will show no improvement after weeks and months, and may even grow worse. Such patients can be cured only when they make up their minds to enter a hospital or to remain in their own homes and follow out a strict dietetic and hygienic treatment. In similar cases I have very frequently obtained a perfect cure by simply removing injurious influences and reforming irrational modes of life, without at the same time instituting any kind of general treatment. It is not improbable that many actual cures which have been made by so-called vegetable specifics, rational hydrotherapy, etc., in cases which defied other methods of treatment, may be referred also to the carrying out of the dietetic and hygienic prescriptions which form a part of these "cures."

Prophylaxis.

After these general remarks, we will now turn our attention to the special therapeutical problems. Should we discover, in an individual who has had contact with a suspicious secretion (after coitus, a medical examination, etc.), even the smallest lesion (a tear, a fissure,

an excoriation) in the part which has been exposed to infection, we must not neglect to treat it thoroughly as early as possible with some caustic, so as to destroy completely any virus which may have entered. Caustics in general are useful for this purpose; but carbolic acid in solid form is to be preferred, a few crystals being rubbed into the injured part. Painting the sore by means of liquefied carbolic acid or other strong caustics may be quite as effective (see Nos. 48–52).* The practically important question, as to how long after the suspicious contact such a procedure may still be effective, is difficult to answer. Sigmund has published a brief summary of observations on this point, but the results are not entirely satisfactory. It is reasonable to assume, however, that the earlier cauterization is effected, the more may be expected of it. After the scab has been thrown off, a perfectly smooth cicatrix is left in most cases, or the cauterization produces a clean suppurating wound, which heals in the usual manner. If the cauterized portion should present an unclean appearance after the scab has come away, a second cauterization is justifiable.

There is some danger to the physician in the present much employed subcutaneous method of treatment of syphilis of inoculating himself by a prick with the hypodermic needle, and syphilis has in fact been inoculated in this way. In my opinion, virus so inoculated would be most effectively destroyed if we allowed the needle to remain *in situ*, and passed through it (say as the negative pole) the current of a galvanic battery, while the other pole, in the form of a sponge electrode, was placed on any indifferent part of the body; a few milliampères passed through for a few minutes would probably suffice to destroy any germs which may have entered. If the needle has already been withdrawn we might attempt to pass a needle electrode into the original puncture, and then destroy the virus electrically in the manner already indicated. It would, however, always be doubtful whether we had succeeded in entering the same point with the needle electrode. Cauterization of the tract of the needle with any kind of (liquid or solid) caustic would be a still more uncertain procedure.

Local Treatment.

The Initial Lesion.

If, in spite of the previous attempts at prevention or without them, an undoubted initial lesion appears, we cannot expect much from its cauterization. In this case, an elimination of the virus

* These numbers refer to the formulæ which will be found at the end of this article.

would most rapidly be obtained by the *excision* or extirpation of the initial lesion—a procedure which was recommended by John Hunter. The occasional removal of chancres (in operations for phimosis and on other occasions) has led us to believe that even when the wound healed by first intention, an induration would recur in the cicatrix and its neighborhood, reproducing the character of the original chancre, and that the further development of syphilis would not be modified thereby. We have, however, now learned that, when we have succeeded in totally excising the initial lesion, the patient is frequently saved from an attack of constitutional syphilis. Since that time this method has been practised by myself and many others. The results have been very variable, but we may maintain on the whole that, in those cases in which the inguinal glands were not yet enlarged, excision most frequently protected the patient against a generalization of the disease. In individuals who already presented enlargement of the inguinal glands this good result was more rare. Some physicians, however, claim even under these circumstances to have prevented general syphilis. In my opinion, excision is to be recommended only when the initial manifestation is present as a perfectly distinct isolated lesion, and is so situated that it may be removed with a wide border of healthy tissue, without causing a malformation or a severe loss of substance; the neighboring lymphatic glands and lymph channels must also as yet be free from involvement, if we are to hope for success. Of course the earlier the patient presents himself for treatment the more likely will the disease be limited to the point of infection. The general practitioner, unfortunately, only rarely has the opportunity to see cases in which this condition is present. The initial lesion may extend downwards or into tissues such as the corpus cavernosum or the glans, so that a successful extirpation cannot be hoped for, or an already existing enlargement of the lymphatic glands renders the prospect of a radical removal of the focus of infection very uncertain. I must, however, confess that in some of my cases syphilis was not aborted in spite of apparently the most favorable conditions and of the exact performance of the excision. The following case especially remains fixed in my memory:

Through an unfortunate occurrence, syphilis was introduced into a family, all of whose members I found suffering with the disease; the husband alone (who had cohabited with his wife, who was also infected eight days previously) was healthy. As a matter of course, I cautioned the man to be continent, and advised him to keep careful watch over himself, and to visit me at once should any suspicious symptoms appear. The following week he consulted me for a red

spot on the prepuce, about the size of a lentil, the appearance of which was not as yet very characteristic; I therefore waited. Three days later there could be no more doubt that we were dealing with a typical initial lesion. This, which was now somewhat larger in size than a lentil, was excised, together with a wide circle of tissue surrounding it, and the wound was closed by suture. The lymph channels seemed perfectly intact. Healing occurred by first intention. About six weeks later I was distressed to find a syphilitic eruption of the skin, and soon after also one in the oral cavity and at the isthmus of the fauces.

Reports of similar bad results have been made by others. Even when no symptoms which can be referred to syphilis are discovered, even after an observation extending over some time, we still cannot exclude the presence in internal organs of minute syphilitic products which do not affect the general health of the individual. But, in spite of this possibility, there are many cases on record in which the cure of the disease could not be disputed. I have myself excised the lesion in quite a large number of cases. Some of the patients whom I had the opportunity to examine later did not present any signs of syphilis for months and years; in others again I could not disabuse myself of the idea that the constitutional affection, which manifested itself in spite of the excison of the initial lesion, ran a milder course than is usually the case. The disease manifested itself by one or two roseola spots only, by a few diminutive papules, or by some insignificant mucous patches. Exactly the same observation has been made by Ehlers. Occasionally delay in the appearance of the constitutional symptoms occurs after excision (F. J. Pick). The fact that we are frequently able by an excision of the initial lesion to eliminate the virus altogether, is quite impressively proved by individual cases in which reïnfection has been observed some time (one or two years) after the operation (Ehlers, Julien).

Such being the facts, I would strongly urge the performance of this small and perfectly harmless operation, which undoubtedly shortens the local course of the disease when the above-mentioned conditions are present. If, therefore, we find the initial lesion distinctly limited, and it can be removed without any mutilation, there being no constitutional symptoms present and no sign that the virus has invaded other parts by way of the lymph channels or by regional migration, excision should be practised, and that to a wide extent, since the gain in a favorable case is very great to the patient, and even in an unfavorable case the resultant wound is exceptionally slight.

In performing the operation a large basin should be placed beneath the pelvis of the patient lying on the table; the part to be operated on is then disinfected, and any existing eroded or ulcerated

spots are touched by lunar caustic. The portion to be excised is now taken hold of, according to its extent, by one or two vulsella forceps—excision forceps—in such a manner that, together with the initial lesion, a strip of healthy skin and subcutaneous tissue about 1 cm. broad is included in the firmly closed jaws of the instrument; now this whole part is drawn away from the penis and snipped off with one movement of the scissors or knife. After thorough disinfection of the wound or cauterization with the Paquelin cautery, and the ligation of any bleeding vessels, a continuous or buttonhole suture is made and an iodoform dressing is applied. For the positive destruction of any germs which may be present in the wound, it would be well, after the excision forceps is applied, to clamp the portion remaining behind at the same time between the blades of a modified Langenbeck's "Deckzange," to cauterize the surface of the wound after the removal of the initial lesion with a Paquelin cautery, and then suture.

Quite frequently operations on the penis which have gone ever so smoothly are followed by an extensive œdema of the prepuce. This œdema can usually be prevented by laying the member on the abdomen and fastening it there by a strip of adhesive plaster, by a band passing from a suspensory bandage, or by a gauze bandage.

As a general rule, the wound heals by first intention, and the sutures are removed in about a week. Should suppuration occur the wound is to be carefully cleansed, covered with emplastrum hydrargyri, with a wet or dry iodoform or other dressing, or treated in some other way in conformity with the rules of surgery.

Locally a successful result has apparently been obtained if the wound heals with a smooth scar. Should induration occur in the latter, we shall have cause to fear that some syphilitic germs have been left behind. If the cicatricial induration presents the same appearance as the original initial lesion, excision may be repeated.

Injections of nitrate of silver in the glands of the inguinal region and mons Veneris, which will presently be described, may be combined with the excision of the initial lesion.

When the initial lesion cannot be exactly delimited or if it is situated in localities, such as the sulcus, corona, glans, clitoris, etc., where extirpation is difficult, any other measure may be tried which has for its object the destruction of the virus. In a number of cases I have made use of *abortive injections* of germicidal solutions into the initial lesion and in the lymph channels connected with it. I have experimented with various preparations (carbolic acid, mercury iodine, etc.), but most frequently use nitrate of silver. By means of a Pravaz syringe I inject a one-half to one per cent. solution of nitrate of

silver into the substance of the initial lesion until anæmia of the skin is produced, and also below and around it, so that the diseased focus becomes well saturated. I then inject 0.1 to 0.2 c.c. of the same solution into the root of the penis or on the mons Veneris, and also in three places in each inguinal region, the skin having been, of course, previously shaved, scrubbed, and bathed with an antiseptic solution. The injection is quite painful, especially on the mons Veneris, but the pain entirely disappears in a few minutes. Further procedures consist in the application of lead water, as the skin of the penis is usually swollen and œdematous for a few days. Occasionally the initial lesion, made anæmic by the parenchymatous injections of nitrate of silver, is thrown off; suppuration, however, rarely occurs, and apart from this there is seldom any marked reaction. The constitutional effects of lues are not always prevented by these silver injections, yet in several patients I was unable, even after years, to find any signs of syphilis, in spite of frequent examinations, and so I feel justified in recommending this comparatively simple measure in selected cases.

If there is no prospect of excising the initial lesion successfully or of destroying it by abortive injections or in any other way—as will more frequently happen in women and in cases of extragenital infection—we shall be obliged to adopt other measures according to the condition and the seat of the point of infection.

In initial lesions of the general integument, the application of gray plaster is most effective, involution of the infiltration occurring under one's very eyes. Ulcerations clear up rapidly, erosions quickly heal. The plaster should be changed according to the amount of secretion present. As a matter of course, we must see that it extends over the borders of the initial lesion and fits the latter as well as possible; this may be accomplished by incising the edge of the plaster. Even where skin and mucous membrane meet, as in the female genitals, the lips, alæ nasi, etc., the plaster may still be employed. For the treatment of initial lesions within the urethra the plaster is to be rolled into a hollow cone with the medicated surface on the outside; then by making two longitudinal incisions at the broad end the one opposite the other, we obtain two reversible flaps which, when the cone is introduced, are turned back and attached to the glans in order to keep the cone in place. The roll of plaster is about 2 cm. long and its apex should be slightly oiled to facilitate introduction. The application should be renewed after each act of urination. This mode of applying the plaster should always be employed in the case of initial lesions of the urethra or of the meatus, for the reason that quite formidable cicatricial strictures may otherwise be formed, even

when no ulceration has been present. The plaster adheres to the inner surface of the prepuce better if it has been smeared over soft gauze.

When the initial lesion is seated altogether or partially within the preputial bag in a case of phimosis or when the initial affection itself has led to such a contraction, triangular pieces of plaster should be applied, after proper cleansing, in such a manner that the pointed end covers the inner lamellæ, and the base of the triangle the outer; or else, what is even more useful, gray ointment is applied directly by means of a small spatula between the foreskin and the glans, and retained by a strip of plaster. After several days the infiltration as a rule will have so far become involuted that the prepuce can again be drawn behind the glans. In cases of very marked phimosis it is a good practice to remove or to expose the lesion by circumcision or splitting of the foreskin. . This procedure is to be recommended if only for the reason that a paraphimosis may otherwise easily occur.

In the latter case reposition can usually be effected when the paraphimosis is of a moderate degree and has not existed too long. For this purpose equable pressure is made on the swollen œdematous glans for a few minutes, so that its size may be reduced, thus allowing the prepuce to be drawn forwards.

When the paraphimotic constriction is too great, a longitudinal incision is made behind it on the back of the penis, through which a hollow sound is passed below the constricting ring, and the incision is then prolonged forwards and backwards until the paraphimosis is overcome. If the latter has existed for some time, an unyielding œdema is usually present, and this makes reposition impossible, even after the removal of the constriction. If reposition is successfully accomplished, the edges of the wound are later approximated by sutures, even when the incision has involved the chancre; but if the incised initial lesion has been ulcerated the wound is to be treated as below described for cases of complications with ulceration.

Initial lesions which have their seat within the vagina or on the portio vaginalis are best treated with unguentum hydrargyri, which may be applied on cylindrical or round cotton pads. To facilitate the removal of the pads, they should be encircled by a thread, which is allowed to protrude from the vulva.

In pregnant women, however, even the smallest pad should not be placed in the vagina. In such a case, good results may be obtained by painting the lesion with an ethereal solution of corrosive sublimate (see Nos. 56 and 57) or by the introduction of suppositories of cacao-butter and mercurial ointment (No. 34).

In initial lesions of the oral cavity, the tonsils, etc., our thera-

peutic efforts will be limited to painting with an alcoholic or, still better, an ethereal solution of corrosive sublimate.

If the initial lesion cannot be excised and is complicated with a venereal ulcer, it is good practice to treat the latter first with an aqueous solution of copper or some other lotion (see Nos. 1 to 3, and 23); or the venereal ulcer is dusted over with iodoform and dressed, until it has disappeared, and not until then is the treatment with mercurial preparations, already described, to be undertaken.

Dressings which may have to be applied to the penis are fastened by one or two turns of adhesive plaster of good quality, or by a narrow gauze bandage. Occasionally it is beneficial to precede the change of dressing by bathing the penis.

Initial lesions accompanied by ulceration, as well as gangrenous forms—no matter where they are situated—should be carefully cleansed (in case of a contracted foreskin by injections) with disinfecting fluids (Nos. 1 to 3), as often as the discharge may make necessary and dressed with iodoform or solutions of copper, corrosive sublimate, etc. (Nos. 1 to 3, and 23).

The urethra should be washed out only immediately after the patient has urinated, for the reason that the urine will carry away most if not all the secretion, while it would otherwise be forced back by the injected fluid; and this is, to say the least, unnecessary.

In cases of the often unavoidable neglect or rough self-treatment which many who are affected by an initial lesion experience, it is inevitable that the lesion should occasionally become complicated in various ways. Diphtheria and gangrene of the focus of infection, or inflammatory swelling and erysipelas of the immediate neighborhood, frequently accompanied by fever, give another aspect to the otherwise characteristic morbid process, and demand a treatment directed primarily to the complications, based upon the known rules of surgery, such as applications of lead water, lotions (see 46 and 47), or iodoform. Only after these complicating symptoms have disappeared may the treatment proper to the syphilitic initial lesion be instituted.

If the initial lesion, complicated by venereal ulcers, gangrene, erysipelas, etc., has its seat within the phimotic sac of the foreskin, or if the phimosis has been caused by the complications, the secretions are dammed back and become hemorrhagic, ichorous, or foul-smelling. In this case the phimosis should be removed at once, the ulcers should be scraped smooth and disinfected, or the Paquelin cautery may be passed lightly over them as well as over the incised surface, sutures should be inserted and the wound should be dressed with iodoform; following this healing by first intention is usually obtained. The application of cocaine to the area to be operated upon

is generally sufficient to produce anæsthesia. It is especially advisable to inject two or three Pravaz syringefuls of a two to three per cent. cocaine solution under the skin at the root of the penis. Or anæsthesia may be induced by Schleich's infiltration method. While the syphilitic initial lesion in a number of cases, especially in women, does not leave behind any infiltrated residue, in others an induration of the tissues at the place of infection remains; but in such cases we are frequently able, by painting the lesion with iodine or covering it with gray ointment, to bring about still further absorption.

The indurated œdema accompanying the initial lesion as a rule also promptly disappears on the application of emplastrum cinereum.

Venereal papillomata are occasionally developed in the course of an initial lesion and also of other syphilitic products on the skin and mucous membranes. These are, as a rule, harmless in themselves, but frequently vex the physican exceedingly by their tendency to return again and again. Formations arising from dendritic growths of the papillæ become larger as a rule and are usually pedunculated, while the papillomata formed by palisade-like cylinders of equal height are sessile and smaller, appearing occasionally in the form of a soft, satiny villous deposit. This last form as a rule relapses even more obstinately than the former. As venereal papillomata are based on the outgrowth of the papillary layer excited by the secretions of disease products, our endeavor must first be to cause the drying up of the discharge, therefore the cure of the gonorrhœa, the ulcerating process, or the suppurating syphilitic lesion. Only after that can treatment be directed against the papillomata with any hope of success. Occasionally in such cases the most simple measures, such as cold applications, cause them to disappear. Several times I have seen these growths contract, dry up, and fall off after keeping them dry and painting them with liquor sesquichlorati alcoholicus (71), or they could then be scraped off with the sharp spoon without causing much hemorrhage and without great pain. These papillomata under certain circumstances are also made to disappear by preparations of arsenic, such as Fowler's solution or the powder which F. Esmarch recommends for carcinoma (69). An alcoholic solution of arsenic (70) which I would call "solutio arsenicalis alcoholica," to distinguish it from the other solution, has proved quite successful in my hands. This is applied to the papillomata by means of a pointed stick of wood, such as a toothpick, in the strength of a one-half to one per cent. solution once or twice daily. The growths may also be covered, when a rapid action is desired, with a bit of cotton dipped into the solution and pressed out. The papillomata even after one such application take on a sodden appearance and become so soft

that they may be wiped off with a cloth. Portions which remained behind are to be treated in the same way until they have perfectly disappeared. If the solutio arsenicalis alcoholica is too recklessly used, irritation of the neighboring healthy tissue will be produced, but this speedily subsides. Papillomata covered by a tough skin demand the application of concentrated arsenical preparations, which should of course be employed with care. Resorcin in powder form or in solution (66 and 67) is also frequently useful. Lactic acid, diluted with a small quantity of alcohol or ether (64 and 65) and applied daily by means of a sharp wooden toothpick, also causes the warts to dry up. Plumbum causticum (63), which is introduced into the papilloma by means of a pointed piece of wood until the former is converted into a pulpy scab, is also very efficacious. The application is painful, but the wart is removed by one application. Covering the papillomata with dry pieces of gauze is necessary after most applications. Very large papillomata, or such as are not caused to disappear by the measures recommended, should be removed by the sharp spoon, knife, or scissors, and the base, skin, or mucous membrane on which they were situated should be touched with the Paquelin cautery; in this case the operation should be done under local or general anæsthesia. Although no positive indications can be given for one or the other method, we may say in general that the liquor sesquichlorati alcoholicus is adapted for small pedunculated papillomata (in which coagulation of the contents of the vessels is most likely to occur), while pedunculated growths of greater circumference and sessile growths are more rapidly removed by arsenical preparations, resorcin, or caustic lead. In general practice, however, the necessity frequently arises of using several methods simultaneously or successively. After a cure is effected the part on which the papilloma had its seat should be kept dry for some time by the application of cotton wool, dusting with starch powder, painting with liquor sesquichlorati alcoholicus, etc.

There comes up for decision at this time the most important question whether or not constitutional measures should be instituted while the initial lesion is under treatment, the object being, of course, to protect against the results of a generalization of the specific virus. It will be better, however, to discuss this point later when we come to a general review of the subject of the therapeutics of syphilis, and we shall, therefore, for the present continue the discussion of the equally important local treatment of the other morbid processes occurring in the course of syphilis.

Lymphadenitis.

In exceptional cases the initial lesion pursues its course without involving the neighboring lymphatic glands; this has attracted my attention especially in the aged, and is probably then connected with senile atrophy of the glands. As a rule, however, the initial lesion is accompanied by a sclerosis of the lymphatic chain and a lymphadenitis. An improvement in the case of the indurated lymphatic cords generally follows painting with tincture of iodine, but an equally good result can seldom be obtained in the case of swollen and indurated lymph glands. Occasionally we obtain a diminution of the glands more rapidly if they are covered with emplastrum hydrargyri, or if small quantities of gray ointment are applied locally. Iodine and the mercurial preparations after an extended local use frequently cause an irritation, and we should in this case allow the skin to heal completely before reapplying the same remedies. In very obstinate cases one or more injections of 0.1 to 0.2 c.c. of a solution of iodine (62) into the enlarged glands or their vicinity will frequently result in a marked diminution in size of the gland. In nearly every case involution, even of large collections of indurated lymph glands, may be obtained by injections of 0.05 c.c. of a fifty-per-cent. solution of gray oil (78). These injections should be made deeply under the skin in the abdominal region, about three finger breadths above Poupart's ligament. A reduction in the size of buboes is effected by subcutaneous injections into the thigh, but injections in this region are well borne only when the gray oil is deposited in very small quantities. I therefore inject 0.01 c.c. of oleum cinereum into each of two or three places at intervals of a few centimetres near the middle of the thigh, and keep the patient under observation for a day or two. The reaction usually rapidly subsides and the resultant infiltration is gradually entirely absorbed.

Should softening and suppuration occur within a nodule of the lymphatic chain or in one of the lymph glands, we should incise the part in its whole extent or enlarge the cavity, scrape it out thoroughly with the sharp spoon, and apply an iodoform dressing. Under this treatment a speedy cure usually takes place. If simple abscess formation is present, puncture followed by the injection of nitrate-of-silver solution, a method which has been practised by me since the year 1892, is to be recommended. The highest point of the abscess is entered by a sharp-pointed bistoury, the pus is evacuated by concentric stroking, and as much of a one-half to one per cent. solution of nitrate of silver (1 or 2 c.c. or more) is injected through a cannula as the cavity will hold. To bring the preparation into con-

tact with all the recesses of the cavity, the small opening is closed by the finger, and the solution is then forced in every direction by the fingers of the other hand. The abscess is now dressed with lead water or iodoform, and a spica bandage or sling is applied. After one or two days any pus which may have reaccumulated is evacuated (if necessary after opening the point of puncture with a probe), more nitrate of silver is injected, and the wound is again bandaged. This is repeated at longer and longer intervals until only a small quantity of a brown or light-colored sticky secretion is formed. When the secretion becomes less, which usually occurs after a few days, an iodoform pad may be placed over the wound and fastened with a piece of well-adhering sticking-plaster. In this way, even when the skin has already become very thin, a cure is usually effected in from one to three weeks. Occasionally the walls of the abscess do not coalesce, and in this case the opening should be enlarged by a blunt-pointed bistoury as far as the periphery of the cavity, and the wound is then dressed in the usual manner. The preceding injections of nitrate of silver in no way retard the healing process. In very large abscesses of the lymph glands, the puncture should be made at both ends, and under certain conditions a drainage tube may be passed through and retained for from twenty-four to forty-eight hours. Apart from this the treatment should be carried out in the way previously described. Simple puncture is also frequently practised; if it is carried out aseptically we frequently meet with good results.

Persisting strumous buboes, presenting as a rule central disintegration, require a radical scraping through a simple or a T-incision (without regard to the presence of any fistulous openings), the ligation of bleeding vessels, ablation of any attenuated loosened portions of skin, in short a real surgical operation. The cleanlier the operation is carried out, the sooner healing will take place. I have many times sutured the wound after an operation of this kind, and not infrequently have obtained union by first intention. In other cases I have succeeded in shortening the time of healing considerably by a secondary suture.

Enlargement of the lymphatic glands occurring in the course of constitutional syphilis does not always attain the size of the initial buboes. Occasionally, however, they become very large, and then require to be treated with iodine and mercurial preparations as described above.

Enlarged lymphatic glands, strumous tumefactions, and gummata as they occur during the later period of syphilis, occasionally complicated by scrofula and tuberculosis, are to be treated according to surgical rules, in addition to appropriate constitutional measures.

Cutaneous Syphilides.

Among the products of the constitutional affection the *roseola* disappears most rapidly, and so thoroughly that it hardly ever leaves permanent changes of the skin behind. The prómpt action of mercurial preparations, particularly blue ointment directly applied, is especially noticeable in this syphilide, although these are applied to the general cutis not so much for the cure of the roseola spots as to influence the constitutional affection.

The macular syphilide, however, does not as a rule make itself felt by any troublesome symptoms, except when it has reached too great an extension, and when it is localized in places rich in sebaceous glands. In that case an intense seborrhœa is developed (on the head, furrows of the alæ nasi, etc.), for the relief of which white precipitate or calomel ointment may be used with good effect. Sometimes a catarrhal condition is developed (as on the prepuce), and such may be benefited by lotions and the application of dry gauze or cotton wool, or bits that have been soaked in a weak solution of corrosive sublimate.

For the *alopecia*, which may occur at any time during the course of constitutional syphilis, local inunctions of blue ointment have given me the best results. These are to be made only at intervals of several days, or are included in the cycle of a general course of inunctions.

Syphilitic *papules* which, when left to themselves, persist longer than the macular syphilide, undergo involution also very rapidly under proper treatment. For the cure of an extensive papular syphilide local treatment is not usually employed, except as the eruption may be touched by the preparation used in the general treatment (in inunctions, baths, or fumigations). Should, however, single papules reach too great a size, and also if they are situated in moist regions where they may become troublesome by the amount of discharge and highly dangerous to other persons; or should they become painful to the bearer by the formation of fissures or ulcers, by their localization in movable parts, etc., local treatment is highly judicious, even unavoidable. *Dry papules* are removed by the application of emplastrum cinereum, calomel ointment, calomel traumaticin (61), or tincture of iodine. For *palmar* and *plantar syphilides*, as also for horny deposits and fine epithelial desquamation, or for papules in callosities, the same treatment may be recommended; or they may be painted with corrosive sublimate collodion (57), or the feet or hands may be bathed in a one-per-cent. solution of corrosive sublimate. Ulcerating papules on the sole of the foot which are sur-

rounded by horny callosities and run a very stubborn course require besides prolonged foot-baths, the shaving or scraping of a layer of the horny infiltrated epithelial border, and this should be repeated if necessary until the surrounding tissues have become soft and yielding; dressings of black gauze (28) and gray plaster will finally bring about a cure. For papulocrustaceous spots and for exuberant papules on the face or elsewhere, white precipitate or calomel ointment is useful. Papules which are complicated with fissures and ulcers (at the anus, between the toes, etc.) are best covered with emplastrum hydrargyri or with oxide-of-mercury gauze. For *moist papules*, cleanliness is the best treatment. The parts should therefore be bathed in carbolic acid, corrosive sublimate, or other solutions, or in sterilized water, and then kept dry by covering them with gauze or cotton wool; dusting them with calomel, salicylic acid, or some other powder (40 to 42) will be found very beneficial. When the discharge is too profuse, sitz-baths of corrosive-sublimate solutions (one-half to one per cent.) are to be recommended, or perhaps later a water-dressing may be used or one of the solutions mentioned above (1 to 5); the lesions then assume a dry form and should be treated as dry papules. Papules which are already *permanently organized* resist milder measures and can be removed only by excision, or destruction by the Paquelin cautery or some caustic remedy (53).

Onychia and *paronychia* accompanied by infiltrations require lotions of corrosive sublimate and dusting with calomel, talcum (40), or the application of a suitable ointment or plaster. When the edge of the nail is overgrown (ingrown nail) small pieces of black gauze (28) which have been cut to a proper shape are to be inserted under the border of the nail with a chisel sound and the wall of exuberant tissue pressed aside with strips of emplastrum cinereum applied like shingles on a roof.

Pustular syphilides require local treatment as soon as the coalescence of the discrete lesions leads to the formation of large or painful ulcers. The mode of treatment is the same here as in the case of ulcers which have arisen from superficial gummata.

Gummata.

Gummatous infiltrations which have not yet softened, or at least have not yet opened, very often go on to involution if they are painted over with tincture of iodine or smeared with blue ointment or calomel traumaticin (61). I have observed gummatous foci of large extent diminish after the subcutaneous injection of one or two drops of some suitable iodine or mercury preparation (62, 88, 90) into the infiltration or its vicinity. Two or three subcutaneous injections,

of 0.01 to 0.02 c.c. of gray oil (78, 79) each, into the parts surrounding the gumma cause marked absorption.

When *ulcers* are already present we may attempt first to scoop out the infiltration which is present at the border and on the base, or to destroy it thoroughly by means of lunar caustic or some caustic solution, following this with the application of emplastrum cinereum, mercurial ointment, a weak solution of corrosive sublimate, oxide of mercury, or iodoform gauze as a dressing. If we find later that the infiltrations have not yet been thoroughly destroyed, or that others make their appearance, the sharp spoon is again employed or the cauterization is repeated. This is more often necessary when lunar caustic has been applied than after the use of a strong corrosive-sublimate solution. Gummatous *cavities* and sinuous *fistulæ* which extend far into the subcutaneous tissue or between fascial layers, usually require to be scooped out with the sharp spoon, and occasionally, also, drainage is necessary. In some cases a definitive cure can be looked for only as the result of a surgical operation. Gummatous tumors which have remained unchanged in spite of prolonged constitutional treatment, extensive infiltrations, and ulcers, for which mercury and iodine have been employed unsuccessfully, may sometimes be permanently cured by extirpation and suture or skin transplantation, in short by surgical measures. I have previously reported cases of this kind.

In cases in which the skin affected with gummata has already taken on a *lupoid* change, which is observed usually after the presence for years of raised cutaneous gummata, a cure is obtained only when the same treatment is instituted as in cases of ordinary lupus. The use of the sharp spoon, cauterization with caustic potash, nitrate of silver, corrosive sublimate, ointment of pyrogallol, or applications of a weak solution of corrosive sublimate, either singly or in combination, will occasionally effect a cure. We shall, however, gain our end here most surely and most rapidly if the lesion is extirpated and the defect closed by suture or a plastic operation.

Gummata of the muscles, the tendon sheaths, lymphatic glands, testicle, or corpora cavernosa are to be treated in the same way as deep gummata of the skin.

Lesions of the Mouth, Nose, and Pharynx.

In syphilitic processes within the cavity of the mouth, nose, and pharynx scrupulous cleanliness and the avoidance of all injuries to these parts are necessary. The patients, unless they wish to suffer endless relapses, should not smoke, chew tobacco, or take snuff. The mucous membranes should be kept free from particles of food

and from inhaled dust by frequently rinsing the mouth and the nasopharyngeal cavity (by means of the nasopharyngeal douche). We shall do well to use plain water for the first ablution of the mouth, nose, and pharyngeal cavity, and to make use of more effective solutions (which are as a rule not devoid of poisonous effect) only after the patient has been taught not to swallow the irrigating solution. Lunar caustic has proved to be especially effective against most of the products of syphilis; it is to be used quite energetically (the pencil being well sharpened) if necessary, every three, four, or six days. In the intervals the infiltrated or ulcerated parts are to be painted with an ethereal solution of corrosive sublimate or iodoform (56, 54); occasionally the painting alone will suffice. In the nasal cavity mercurial ointment, oxide-of-mercury gauze, cornucopias of emplastrum hydrargyri with the surface of the plaster turned outwards (in the same way as the cones are employed in the case of chancre of the urethra), or medicated bougies (38, 39) may be employed. It goes without saying that the parts should be freed from adhering mucus or pus previous to institution of the local treatment. The use of the mirror in the treatment of the nasal and pharyngeal cavity is quite advantageous and even occasionally indispensable.

The Larynx.

Syphilitic catarrh of the larynx usually improves rapidly with inhalation of tannic acid, alum, or corrosive sublimate spray (10, 20, 24), and occasionally the cicatrization of ulcers and the involution of large infiltrations may be effected in this manner. In obstinate cases preparations which stimulate absorption or cauterize may be directly applied to the parts with the aid of the mirror. Michael Grossmann, who also lays great stress on local treatment, uses the galvanocautery (under cocaine anæsthesia) nearly exclusively whenever he finds an indication for cauterization in syphilis of the laryngeal, nasal, or pharyngeal cavity. The result, in his experience, cannot be compared with that of any of the older methods of treatment by caustics. He cauterizes only ulcers and severe and obstinate infiltrations which will not respond to any other treatment. In all other forms of nasal or laryngeal syphilis, and in the case of ulceration also in the intervals of cauterization, he says that he has for a number of years exclusively employed oleum cinereum. The results of this method of treatment, which, of course, was conjoined with constitutional treatment as the most important part, were very satisfying. Grossmann says, indeed, that he knows no remedy which will more favorably influence the local syphilitic process in the larynx, the nose, and the pharyngeal cavity than oleum cine-

reum. In a short time, often after a few days, the subjective symptoms, as the troublesome sensation of dryness, the irritation producing cough, the difficulties of deglutition, the pain, etc., begin to improve. The objective symptoms subside somewhat later, and the disappearance of the infiltration, the clearing up of the ulcers, and the diminution of the swelling may be observed even when the formation of a perichondritis would naturally be expected on account of the intensity of the symptoms.

External applications to the throat in the neighborhood of the larynx (tincture of iodine, mercurial plaster, the subcutaneous injection of a drop of gray oil) quite frequently are of indisputable service in the treatment of laryngeal syphilis.

The Rectum.

The local treatment of syphilitic affections of the rectum, the vagina, and the uterus should not be carried out with less care. The remedies are most easily applied to the *rectum* in the form of suppositories or of small clysmata (35, 36, 63). With the aid of a speculum or gorget, however, any remedy recommended for application to the mucous membranes may be employed. Syphilitic ulcers having their seat in the rectum or the anus (from initial lesions or other processes), which had long resisted treatment, have rapidly healed after incision of the sphincter.

The Vagina and Uterus.

In the examination and treatment of the vagina, the portio vaginalis, and the cervical canal I employ by preference Z-shaped spatulæ or specula of that shape; in this manner every recess and fold can easily be examined and treated locally. When no assistant is present a simple cylindrical or moderately conical (according to Ferguson) or three-bladed (according to Meadow and others) speculum may be used. For the removal of discharges and the local application of solutions to diseased portions I employ, for the sake of cleanliness, a caoutchouc rod, around one roughened end of which a pledget of cotton-wool is wound. I keep these pencils on hand in various sizes for use in the oral or nasal cavity, etc. If ointments or solutions are to be applied for some time, cylindrical or round cotton pads or tampons are employed. Care must be taken to protect the surrounding parts when areas of limited extent are to be treated with caustic remedies. Mercuric-oxide or corrosive-sublimate gauze has frequently given good results in the treatment of syphilitic ulcers of the cervix. Pregnant women bear gray globules (34) with most comfort. Irri-

gations with solutions of alum, carbolic acid, and other medicaments should be employed according to the amount of suppuration present. When a purulent catarrhal secretion of the vagina accompanies the lesion, it is of special value to insert once or twice a week a long tampon well dusted with powdered alum or saturated with a strong solution of sulphocarbolate of zinc (25, 26), ichthyol, etc., for half an hour or even longer.

The Bones and Joints.

We should endeavor in syphilis of the bones and joints to promote absorption by the local or regional application of preparations of iodine or mercury. The joints should be immobilized when necessary, and large gummatous infiltrations may occasionally be scooped out with advantage and drained (H. Leisrink and A. Alsberg). Resection has not always given good results.

If *necrosis* has occurred in the course of syphilis, we should see that the pus is freely evacuated, and then wait until the sequestrum becomes loose. The dead bone is as a rule thrown off spontaneously (as in the nasal cavity), or extraction may be accomplished very easily; in exceptional cases only the sequestrum will have to be cut away by means of instruments. We should be in no hurry to remove the diseased portion in necrosis of the bones of the skull, but should give the dura mater an opportunity, by a gradual callous thickening, to take the place of the necrosed bones. It is a rational procedure to incise the soft parts radially and strip them up from the bone a little beyond the border of the diseased parts. The denuded healthy white bone will in a short time assume a rosy color from hyperæmia and new formation of vessels, and will at once become covered by granulations. The inflammation of demarcation grows more intense and the loosening of the sequestrum is thus expedited. Should further observation indicate that the necrosis affects only the outer table of the skull, the process may be materially shortened by cutting away the dead lamella. In cases, however, in which the lesion of the bones of the skull causes a morbid change in the meninges or the brain, trephining is indicated in order to relieve pressure on the brain, or to give vent to the pus accumulated on the inner surface of the skull. Many hints for the guidance of the physician in dealing with syphilis of the bones of the skull will be found in the foregoing. As large defects of the bone, as a rule, are replaced only by a cicatrix (probably dense, it is true) of the soft parts, we should never neglect to cover the latter by a leather or rubber plate so as to protect the brain still better against any possible mechanical injuries. After the wound has healed, the advisability of a

plastic operation and the implantation of plates of celluloid or decalcified bone may be considered. If a perforation of the *palatal process* of the upper jaw has resulted from a syphilitic necrosis, an opening will be formed between the mouth and the nasal cavity which will result in a disturbance of speech, and will also interfere with the formation of the bolus of food and with deglutition. Injuries of this kind should therefore be closed after cicatrization has taken place either by a plastic operation or by an obturator. Perforations the diameter of which i not greater than 1 cm. may be closed by a well-fitting bean. This will swell somewhat in the oral cavity and thereby fulfil its mission even better. The patient soon learns to place the bean, by the help of the tongue, into the proper position.

In *spondylitis syphilitica* we shall have to employ, in addition to local applications of iodine or mercurial preparations, those mechanical auxiliaries (horizontal position, plaster jackets and similar supports) which are indicated in the individual case.

The Eyes and Ears.

In syphilitic affections of the auditory and visual apparatus, a local treatment of these organs of sense by the instillation of oleum cinereum into the external auditory canal or the conjunctival sac is possible, and in choroiditis, iritis, etc., it is directly indicated. In this case regional applications of specific preparations (for example, on the temples) may also be attempted. Those measures should also be taken which are considered indispensable in non-syphilitic affections of the eyes and ears.

Internal Organs.

Among the internal organs the local treatment of the *intestinal tract* can seemingly be best carried out by internal medication, which is to be considered later on. We should not, however, overlook the fact that every form of constitutional treatment by mercury (the cutaneous and subcutaneous as well) will exert a powerful influence on the intestine, for the reason that a great part of the ingested mercury enters it and is excreted by it. In the same manner a local action by the administration of specifics may certainly be obtained in affections of the *kidneys*, as mercury is freely (perhaps most freely) eliminated by this organ. Some tissues, as we shall learn later, possess a great affinity for mercury; the *liver* may be classed with these, and to a less degree the *spleen*. Accordingly a special, so to speak, local action on these organs may be obtained by a mercurial treatment.

In the case of other tissues (bones, muscles, lungs, brain) which have only a very slight affinity for mercury, we find ourselves less favorably placed. It is possible, however, that inflamed tissue may possess a greater affinity than normal tissue for the mercury circulating in the blood—it has in fact been found in the blood in considerable quantity. In an experiment made by K. Ullmann at my suggestion, an artificial callus showed a decidedly stronger reaction for iodine and mercury than the normal bone. It is possible, therefore, that a gumma in the *brain* or the *heart* may contain more mercury, during a mercurial course, than the normal parts.

The Respiratory Tract.

In syphilis of the bronchial tubes and of the lungs inhalations of mercurial preparations in the form of vapor may be used. The managers of sanatoria and hospitals ought to facilitate this mode of treatment by making special inhalation-chambers (small closets or sedan-chair-like boxes). The inhalation of medicinal substances, by means of a portable apparatus such as is used in laryngeal affections, is not indicated in lung affections, being too laborious.

Here and there gummata of internal organs, mistaken for malignant tumors, have been extirpated. The liver also has been operated upon in consequence, of an error in diagnosis, and the results in some cases were good (Julius Hochenegg, H. Tillmanns). The removal has been accomplished, after trephining, of a gumma from within the cranial cavity on which specific treatment exerted but little effect, and after this antiluetic treatment has effected a cure. Affections of the brain or meninges as a result of syphilitic processes of the bones of the skull, occasionally urgently require trephining, and in a few cases the life of the patient has been thus saved.

Constitutional Treatment.

It is impossible for us to discuss all the remedies which have been recommended for this disease, and we shall mention only a few preparations which are used with success under the restrictions previously mentioned. Mercury and iodine among the metals are the most commonly employed. Our idea is to incorporate the preparations derived from these with the diseased organism by way of the intestinal canal, the skin, or the subcutaneous tissues.

Mercury.

Mercury has up to the present day remained the sovereign remedy in syphilis. When this is supplied to the body in any way it exerts

such an influence on all the tissues that the constitutional disease in the great majority of cases heals in a manner which borders almost on the miraculous. We shall call the treatment which is adopted at any period of constitutional syphilis the *temporary* one. It has been observed, however, that mercury, when administered immediately after the appearance of the initial lesion, also modifies the system (and perhaps the virus as well) in an unmistakable manner. In the hope that the disease might in this manner be aborted, or at least rendered milder, a constitutional mercurial treatment, *preventive medication*, has been employed very early, even before the appearance of constitutional symptoms.

We shall first discuss the *temporary* mercurial treatment, as being by far the most important, and shall begin at once with that method which has long been the method of choice in the treatment of lues, and which on account of its efficiency is still highly recommended. I refer to *inunctions* (frictions, rubbing) with blue ointment, simply called the inunction method.

The most effective preparation of mercury which we incorporate with the body by way of the absorbing skin is even now the *unguentum cinereum* (75, 76); its composition with unimportant modifications in the course of time has remained pretty much the same. The base for the ointment, which was recommended by Oscar Liebreich, namely lanolin, possesses the great advantage of very easily penetrating the horny layer of the skin, but it cannot be used on the parts of the skin that are but slightly hairy so well as fat. In recent times many other fats have been used in preparing blue ointment. Unguentum cinereum is rubbed daily or every second day into a fresh part of the skin for twenty minutes, and even longer, in doses of from 0.5 gm. in children to 2–4 gm. and more in the adult, until the amount applied has entered the skin. The more the hairy portions of the skin are avoided the better will the ointment be borne, and the softer the skin is the more voraciously will the ointment be taken up by the latter. A bath should, therefore, previously be taken by the patient, and we should see to it that a new region is anointed each day. To facilitate this, the whole surface of the skin is divided into several regions, and the inunctions are then made in the following order: First inunction, the flexor surfaces of both forearms; second inunction, the flexor surfaces of both legs; third inunction, the flexor surfaces of both arms; fourth inunction, the inner surfaces of both thighs; fifth inunction, both groins; and sixth inunction, the back.

When the end of the cycle has been reached, it is to be renewed as often as necessary. But we should not neglect to order a bath to be taken at least before each inunction, so that the skin is freshly

cleansed and thus is prepared for the absorption of the mercury. We shall, of course, at times depart from this schedule, according to the seat and distribution of the syphilitic products, in order that we may the more freely and more frequently anoint diseased portions than others which are less involved or perfectly healthy. Inunction will be most perfectly accomplished, if the ointment is rubbed with even pressure into the parts with the ball of the thumb in long elliptical figures. The nurse who has charge of the rubbing should, as a matter of precaution, wear gloves of leather or rubber. In place of the hand or the ball of the thumb we may substitute an "inunctor" made of hardwood in the shape of a mushroom with perfectly smooth surface. We use this by taking the handle in the fist and rubbing in the ointment with the convex top, which is usually covered with leather.

In order to insure a subsequent even temperature, which is favorable to the inunctions, I prefer to have them made at night before the patient retires; much sweating is not desirable.

Patients who are otherwise strong enough may practise the inunctions themselves. The amount of ointment required should first be smeared on the balls of both thumbs, and then the left arm is rubbed by the right hand and the right arm by the left hand according to instructions. Inunctions on the back must necessarily be made by a second person. In greatly debilitated patients inunctions are not well borne and oftentimes cannot be made. Certain affections of the skin may also constitute a contraindication to inunctions—such are extensive ulcerations, painfully inflamed nodes, severe ichthyosis, pityriasis rubra pilaris, and similar dermatoses producing profound changes; psoriasis is nearly always made worse by inunctions.

Certain cutaneous affections which may complicate syphilis, but which are curable, such as erysipelas, erythema, eczema, or scabies, should be first cured before the inunction treatment is attempted. On the other hand, the general contraindications to the use of mercury in any case, which will be discussed later, should receive careful consideration.

Occasionally the contraindication may declare itself during the course of inunctions. Thus the latter may now and then produce eczema (eczema mercuriale), or in rare cases folliculitis. Milder eruptions frequently disappear and do not prevent the continuation of the treatment, but should they become more intense, extending to larger cutaneous areas, there is nothing left but to stop the inunctions. Occasionally an attempt made later will succeed after the eczema has run its course, the skin now having a tolerance for the process. Should the second attempt, however, react with an eruption, further efforts in that direction must be abandoned.

In rare cases the use of blue ointment is forbidden by the appearance of an erythema which occasionally presents a toxic character. The site of the application becomes of a vivid red color and shows more or less inflammatory infiltration, and in addition to this there is an increased desquamation, or the exudation is increased to such an extent that vesicles and even large blebs and pustules are raised, or punctiform hemorrhages may sometimes be observed in the skin. Itching and burning sensations are not always markedly present; restlessness and a general discomfort are more frequently experienced. Occasionally the erythema extends over the whole body, and its eruption is accompanied by slight fever. After a few days the swelling decreases, the vesicles and blisters dry up, the skin becomes paler and begins to wrinkle, and in severe cases a broadly lamellated desquamation ends the process. The toxic exanthemata produced by other modes of giving the mercury will be referred to later.

Aside from this the indications for inunctions are very numerous. The method may be used in children, adults, and the aged, and the action on the syphilitic process is as a rule excellent and permanent. The effect may be increased or diminished according to the size of the dose. The permanency of the result is probably based on the fact that mercury taken into the body in this manner is only very slowly eliminated. The researches of Paschkis and others have shown that traces of the mercury can be found in the body for years. In the case of one of my patients who had received seventy inunctions early in 1892, and who took iodine only later, traces of mercury were still found in 3,350 gm. of urine analyzed in Ludwig's laboratory at the end of March, 1895. In another patient mercury could still be detected ten years after the last course of inunctions.

Some look upon inunction as undoubtedly the most effective method of administering mercury. This, however, does not seem justified either by theoretical observation or by practical experience. Cases in which inunctions are ineffectual and in which subcutaneous injections only produce results have frequently occurred in my practice and in that of others (Nickolich, Thibièrge, Besnier, Mannaberg, Jullien, Mendel, and Wickham). It is probable that the skin of some individuals is less suited for the absorption of mercury than that of others.

In what way is the mercury absorbed in inunctions? The startling effect which inunctions exert on the syphilitic process naturally excites curiosity as to how the mercury is absorbed. Primarily we think of an absorption by the skin. Microscopical sections of skin which has had blue ointment rubbed into it, shows the presence of particles of mercury in the hair follicles and ducts of the

sebaceous and sweat glands. The metal is therefore forced mechanically by the inunctions into the pores of the skin, perhaps even more deeply, and there it experiences the chemical changes necessary for absorption. It has, however, also been determined by clinical observation and repeated researches in this direction that the mercury contained in the ointment becomes vaporized and is then undoubtedly absorbed in the form of gas, and that to such a degree that occasionally the nurses and even the friends of patients (as Welander and others, myself included, have seen) are attacked by more or less distinct symptoms of mercurial poisoning. In one of my cases the vaporized mercury could even be detected in the urine of an occupant of the same room who was not directly being treated with mercury, but who nevertheless was cured of his luetic lesions.

Experiments relating to this have led Edward Welander to believe that the amount of mercury absorbed in the gaseous form is quite considerable. On the strength of his own experience, and on that of a great number of observations made regarding the clinical symptoms as well as the excretion of the mercury in such cases, Welander has recommended simple *smearing* with blue ointment as a method of treatment for syphilis, which is as simple as it is effective. I have made use of this method in a great number of patients and found that the syphilitic symptoms very promptly disappear. From 4 to 6 gm. (℥ i.–iss.) of blue ointment is spread by means of a spatula or the handle of a spoon over the cutaneous region on which otherwise inunctions are made, a muslin or gauze bandage is then loosely applied or the part is bound up in a cloth, and the patient is kept in bed, lightly covered, for from ten to fourteen hours. He is then placed in a bath, or the skin at least is washed with soap and water. On the following day this is repeated on another portion of the skin, and the same routine is observed as has been described in the case of inunction. These applications are also best made in the evening. The mercury in this case is undoubtedly absorbed in the form of vapor, and in all probability through both the skin and the respiratory tract, although it is difficult to decide which one of the two organs plays the most important rôle.

The smearings may also be combined with inunctions, so that one-half of the ointment (3 gm.) is rubbed into the skin, and the other is merely smeared over the same portion. The rest of the treatment is to be conducted according to the directions just given. The indications for this mode of application are fairly liberal. Weak and debilitated individuals who have been much distressed by one inunction are very well able to bear the simple applications; ulcerated and tender cutaneous nodes, as well as many dermatoses (ichthyosis,

pityriasis rubra pilaris, etc.), which contraindicate inunctions, bear this method of treatment very well.

It is questionable whether the results of this mode of application are as permanent as those of inunction; for while in the latter particles of mercury penetrate the skin and are retained in the tissues for quite a time, this does not happen when the ointment is simply spread on the skin. The application of mercurial soap is very similar in its effects to the combined methods of inunction and smearing.

The constitutional treatment with *mercurial plaster*, of which great things were formerly reported, has been revived in recent times by Unna. This method has been very successful in my hands in a number of cases. I have found it to be particularly useful in children. I apply strips of emplastrum hydrargyri of the width of two or three fingers over the skin of the upper extremities in the direction of their long axis (strips encircling the limb constrict it) and over them loosely apply a gauze bandage. At the end of a few days (from four to eight) the plaster is removed and the arm is bathed and dusted with powder (41, 42). Then the second arm is plastered, and after a further period of four to eight days, one lower extremity, following this the other leg, and then the trunk. If the treatment is to be continued, we return to the arm and follow the same succession. It is exceedingly important to cleanse the skin before applying a fresh plaster. According as we wish to make a more intense or a moderate impression, a pause of one to four days may be made between the plaster applications.

If the plaster is properly made, we need not fear any irritation of the skin; even when itching occurs in the first few days, this usually disappears very quickly and does not necessitate the discontinuance of the plaster treatment. It is remarkable that the absorption of mercury appears to go on even when the plaster is not renewed for a long time. I have been able to convince myself positively of this, although the traces of mercury in the body cannot be found so distinctly or for so long a time as after inunctions. The plaster treatment constitutes a mild mercurial course with a good and equable effect, and is therefore especially applicable in the treatment of syphilis in children as well as in adults, especially when local absorption is desired together with the constitutional effect. The presence of extensive ulceration is no absolute contraindication to the employment of the plaster. If the ulcers are filled with oxide of mercury gauze or corrosive sublimate gauze (28) and then covered with plaster, the secretion will be absorbed by the former while the action of the plaster is not prevented.

Quinquaud has recommended a *calomel plaster* for the same purpose. *Calomel traumaticin* (74) has also been used in syphilis and found to be quite effective. In my experience the general effect of calomel traumaticin is a mild one, but the mercury is quite certainly absorbed, as its presence in the urine proves. I order the application to be made two to three times a week, each time on a different part of the body.

Fumigation has also been employed in order to obtain cutaneous absorption of the mercury for its constitutional effect. This method of treatment, which seems to be a favorite one in the Orient, has also been repeatedly advocated by individual physicians (Henry Lee, Heinrich Paschkis), without, however, gaining any permanent vogue. In the absence of formal apparatus for the giving of mercurial vapor baths, fumigation may be carried out in the following manner: The patient, after having disrobed and taken a bath, is seated on a chair with a perforated seat; below this a tripod is placed, on which is a saucer containing the calomel; this is heated by means of an alcohol lamp. Now the patient is covered by a cloak which envelops the entire apparatus as well; this is made of some heavy material or rubber into which several hoops have been sewn so as to leave a certain amount of space around the body of the patient in such a manner that only his head is exposed. When the lamp beneath the tripod is lighted, the mercurial vapor completely fills the space underneath the cloak, and is deposited on the patient's skin. For the production of this mercurial vapor, calomel is the most suitable preparation, 5 to 10 gm. being placed in the saucer; to this vapor the body is exposed about fifteen minutes. At the end of the fumigation the patient is placed in bed, where he should remain several hours, after which he may dress. The fumigation is repeated daily.

The attempt to secure a constitutional effect by means of *corrosive sublimate baths* has gained more adherents. These baths are effective only when the patient remains in them for quite a long period.

I have frequently employed them successfully in the case of children and infants. Corrosive sublimate baths find their indications, especially in the treatment of mucous patches, pustular and ulcerating processes, that is to say, cutaneous syphilides. Marked constitutional effects cannot be obtained by this method, probably for the reason that absorption is in general too slight.

Of incomparably greater efficiency are corrosive sublimate baths conjoined with *electrical cataphoresis*. For this purpose we may use Gaertner's bath of two cells, which should be divided by a properly fitting diaphragm separating the two cells. Each cell is attached to

one pole of a battery consisting of about fifty large Leclanché elements; the box which contains the battery is supplied with a finely graduated rheostat, a galvanometer, and a current changer. To the bath, which should have a temperature of 35° C. (95° F.) is added from 12 to 15 gm. of corrosive sublimate, which should be thoroughly dissolved. The patient is then placed in the tub, the diaphragm is put in place, the poles are attached, and the current is gradually increased by means of the rheostat to from 100 to 200 milliampères, and is allowed to pass for fifteen minutes. We then reduce the current by way of precaution, reverse it, and again increase it with care to from 100 to 200 milliampères. At the end of fifteen minutes more the current is shut off and the bath is now finished.

The remarkably favorable influence of these electric sublimate baths on the syphilitic process has been observed by me in numerous cases. An examination made at the same time by A. Kronfeld, of my clinic, to determine the excretion of mercury, demonstrated that by this method of treatment a large quantity of the metal is absorbed and elimination is equalized. I have not observed any inconveniences from the baths; their application is moreover clean and very easily made. The only objection to their general use that could be urged is their price. As regards the permanent deposit of mercury in the tissues, nothing is so far known.

A discussion of the *subcutaneous injection* of mercurial preparations most naturally follows that of the cutaneous treatment. The first who employed this method were Ferd. v. Hebra, Scarenzio, and Berkeley Hill. The real incentive to the extensive employment of subcutaneous injections was, however, given by George Lewin. Since then this method of treatment has always been in order, and has been improved in many ways by numerous observers. The number of mercurial preparations recommended for this purpose has grown enormously up to the present day. They are suitably divided into the *insoluble* (or at least slightly soluble) and the *soluble* mercurial preparations.

The injection of insoluble preparations has been rendered practicable by suspending them in glycerin, water, mucilage, or oil. Let us say in passing, that the inconveniences of the subcutaneous injection of mercury are very greatly reduced by the use of oil or any other kind of fat. I was the first to demonstrate this when I introduced the preparation known as gray oil (1884). The great disadvantage, however, of the suspension of mercury in oil is that the metal will at once begin again to sink to the bottom, no matter how energetically it has been shaken, and an exact dosage is therefore out of the question. According to the researches of K. Ullmann errors in

the dosage of subcutaneous injections, reaching as high as ninety per cent., may thus be made. As the mercurial suspensions which are used for injections contain a high percentage of metal, inaccuracies to such an extent should be if possible avoided. This fact caused me to introduce a mixture of lanolin and liquid vaselin—(paraffinum liquidum), which remains solid at ordinary temperatures and becomes semisolid (*i.e.*, suitable for injections) only when heated. The mercury to be used is well rubbed up with this mixture, and remains equally divided in the solid preparation, and then may be taken up by the syringe immediately after being heated in quantities which furnish an exact dosage.

A well-made and exactly graduated syringe is here of the greatest importance. The hypodermic syringe which I have employed for years is constructed in such a manner and so arranged that an exact dosage down to 0.01 c.c. is possible. Those found in the trade are usually not made after an exact standard (occasionally they are even one-third too large). To be able with ease to inject as small a quantity as 0.01 c.c., my syringe is made so that, although of the usual length, it holds only about 0.5 c.c. It is now determined by chemical scales exactly how much distilled water the instrument will hold. Assuming that this quantity is 0.48 or 0.54 (after an average of ten weighings) forty-eight or fifty-four lines or dots are made on the piston rod and 0.1 and 0.5 c.c. are also especially marked.

The syringe and needle should be disinfected, even when it arrives newly from the instrument maker, by having a three-per-cent. solution of carbolic acid passed through it, and after the wire has been inserted and the needle has been dried with a piece of aseptic gauze, it should be permanently kept in a glass case containing liquid vaselin.

I shall now describe the method of injection with a preparation which in its composition as well as in its effect approaches most nearly to mercurial ointment, namely, gray oil (oleum cinereum).

Gray oil, which was introduced into therapeutics by me about fifteen years ago, is an intimate mixture of fat, oil, and metallic mercury. I now use almost without exception a fifty-per-cent. preparation, but ocasionally one of thirty or twenty per cent. strength. It is well first to prepare a basic ointment, consisting of lanolin and mercury, and after this by admixture with oil to prepare the oleum cinereum for use in the injections.

For this purpose lanolin is dissolved in a large quantity of chloroform, and rubbed up with mercury; we then add to the latter a double quantity of lanolin.* As the chloroform evaporates during tritura-

* The trituration of the metal may be said to be perfect when a small portion,

tion a mercurial ointment in the proportion of two to one is obtained —"Unguentum cinereum lanulatum forte" (77).

This basic ointment, which contains mercury in excess and less lanolin, is used for the preparation of an oleum cinereum containing fifty per cent. of mercury. This preparation containing fifty per cent. consists of two parts of mercury and one part each of lanolin and oil (78). The oil containing thirty per cent. of mercury is prepared after formula No. 79.

The gray oil should be kept in a small wide-mouthed bottle of a capacity of 10 to 15 gm., supplied with a well-fitting glass stopper, and is placed in a larger powder jar impervious to air and dust and kept in a cool place. During the hot days of summer the powder jar may be placed in a vessel of cold water, if an ice-box or other cool place is not at hand, the water being renewed two or three times daily, and the oil is thus kept solid.

The preparation is warmed over a spirit lamp when it is to be used, and repeatedly shaken up until the oil has become semifluid and suitable for injection. Karl Ullmann, who has made interesting researches in the laboratory of Professor Kratschmer in regard to this gray oil, recommends a temperature of 23° or 24° down to 20° C. (73.6° to 68° F.) as the temperature in which the preparation containing thirty and twenty per cent. of mercury is ready for injection. There is, however, no harm in exceeding this temperature, which in practice is probably always the case, because we are taught by Ullmann's researches that oleum cinereum, if it is shaken up later and kept in a cool place, will again contain the mercury equally distributed.

After the injection has been made the bottle is again closed. Any gray oil which may have adhered between the stopper and the neck of the bottle is wiped away with a piece of gauze (after the bottle has been warmed and shaken up if necessary), and the preparation is again set in a cool place or in cold water; if treated in this manner it may be kept fit for use for weeks.

In the hospital, where larger quantities are used, the gray oil is prepared fresh every week.

The "basic ointment" is best manufactured by the druggist. Experiments made in my clinic have shown that we are perfectly justified in making use of a basic ointment that has been prepared six months previously. It is, however, taken for granted that the preparation has been kept in a cool place. In country practice and in

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thinly spread by means of a thin-edged iron spatula, on a dark piece of paper does not show any globules of mercury when carefully examined under a magnifying glass.

localities where the ointment, for any reason, cannot be carefully prepared, its great value is found in the fact that it may be kept in sufficient quantities for from three to six months' use if made by some reliable apothecary. The further preparation and treatment of oleum cinereum is, moreover, comparatively easy. It is only to be premised that all manipulation should be carried out with that cleanliness and care which a preparation used for subcutaneous injections necessitates.

The amount of mercury present in a cubic centimetre of a fifty-per-cent. preparation of gray oil is, according to Ullmann, 0.810 gm.; hence twice as much as is contained in an equal volume of a thirty-per-cent. preparation, which contains 0.369 gm. of the metal; therefore only about one-half the quantity of the fifty-per-cent. solution should be injected as of the thirty-per-cent. preparation.

I never inject more than 0.05 c.c. of the fifty-per-cent. preparation of the gray oil, which is the one that I almost invariably use in the constitutional treatment of syphilis, so that unless otherwise specified a preparation of fifty-per-cent. strength is always meant. The dose for an injection as mentioned is always 0.05 c.c., *i.e.*, 0.04 gm. of metallic mercury. The first doses, when we are dealing with constitutional syphilis, are administered every second or third day, that is, about twice a week. If the symptoms diminish and improvement is marked, the injection is made only once every five or eight days, and after a perfect cure has been obtained, one or two doses are administered at the end of ten to fourteen days as a supplementary treatment. For a thorough mercurial course, from eight to twelve, rarely more doses are necessary, while for the cure of relapses from four to six are sufficient.

The physician must, of course, exercise his judgment as to how far he may deviate in regard to the dose of oleum cinereum in special cases in the treatment of constitutional symptoms. He must not lose sight of the fact, however, that there should be a limit to the number of injections of gray oil, and to the frequency of their repetition, since the mercury is usually absorbed slowly and its cumulative effects might be serious.

In grave individual cases (syphilis of the nervous system, lues of the nasopharnygeal cavity, etc.), in which I was compelled to continue antisyphilitic treatment with mercury for some time, or to repeat it, I always allowed a pause of several weeks to intervene after injecting 0.6, 0.7, or 0.8 c.c. of gray oil, and when a repetition was necessary, that is to say, when the treatment had to be begun again, I gave as a rule only 0.05 c.c. in the course of one or two weeks.

I almost invariably make the injections in the back and deep under the skin. The injections never excite suppuration if we avoid piercing the skin a second time with the penetrating point. A swelling of the size of a hazelnut is formed in the back on the second or third day after the injection, and the patient experiences a sensation as though he had received a blow in that locality; after a few days the swelling and tenderness diminish and finally disappear altogether. The subsequent injections are frequently not felt at all by the patient, or only in a slight degree.

A small percentage of patients (more frequently women than men) complain of a slight feverishness, which makes its appearance on the same day in which the first injection is administered, and which only very infrequently recurs on the following day. In cases in which the temperature was taken it was found to be raised several tenths of a degree, even as high as 39° C. (102.2° F.) and over. Occasionally a slight fall in the temperature is noted. The subsequent injections are as a rule not followed by this reaction.

The injection is made in the following manner: A clean cloth (handkerchief, napkin, or even a sheet of white paper) is spread out, and on it the instruments necessary for the injection are placed (clean pieces of gauze, saucers, etc.); the syringe and needle are taken from the liquid vaseline and carefully dried; the gray oil, slightly warmed, is shaken up slowly, drawn into the syringe, and again rapidly expelled, so as to get rid of air bubbles; the syringe is then filled again with the preparation, 0.1 c.c. more than we wish to inject being taken up. The needle is now turned upwards and the piston is pressed upon until the gray oil makes its appearance at the point of the needle. The piston is then set, and the marker is screwed forward to the mark denoting the volume 0.05 c.c. which we wish to inject; then the gray oil which adheres to the needle and the syringe is wiped off with a clean rag, a thick fold of the skin of the back is taken between the index finger and the thumb of the left hand * parallel to the median line, and the needle is pushed deeply under the skin in the direction of the fold, in front of the thumb and index finger. The fold is now released, and by displacing and rolling the skin we can satisfy ourselves that the cutis is not caught in the point of the needle. The base of the needle is then steadied by the fingers of the left hand, and after having convinced ourselves that the needle is firmly fastened to the syringe, as much of the fluid contained in the syringe is injected as is indicated by the marker. The needle is then removed and the tip of the finger is pressed for a moment on the

* In the hospital I always order the skin to be washed before each injection; in private practice this is usually neglected.

opening made by the needle. Massage or stroking at the point of injection is unnecessary. After the injection has been completed, the oil remaining in the needle and syringe is emptied out. Both needle and syringe are cleaned out with liquid vaseline, a wire is inserted in the needle, and the instrument is again replaced in the liquid vaseline.

Should a few drops of blood appear after the removal of the needle, the finger is held somewhat longer over the spot where the needle had entered. Occasionally a slight subcutaneous hemorrhage takes place, which is shown by the fact that the skin bulges out in the form of a protuberance the size of a nut immediately after the injection. This slight hæmatoma does not complicate the injection at all, and is perfectly absorbed, even when the spot presents fluctuation for a time, generally passing through the well-known series of discolorations. It is well to begin the injections at the junction of the neck with the back, or somewhat lower, perhaps 4 cm. to the left of the median line, and to make the subsequent injections on the same vertical line about 4 cm. apart, so that five, or at the most six, injections will be made on one side. I usually stop before reaching the region of the belt on account of the tightly fitting clothes which make pressure here. The other injections are made similarly to the right of the median line. These injection lines may be designated as "medial."

Should a case necessitate more injections (twelve or more, which only rarely happens, however), these are distributed in a line of injection lying more to the outside, about 8 cm. distant from the spinal column—"external lateral"—within which region the injections are made, also through a vertical distance of 4 cm.

It is well to raise the cutaneous fold in an oblique direction and to insert the needle obliquely but deeply under the skin over the fossa supraspinata (the first point of injection in the "lateral" vertical line), bearing in mind the directions previously given.

In persons who possess a very abundant layer of adipose tissue we shall frequently be unable to pick up a cutaneous fold in the back; in that case I insert the needle in an oblique direction as far as the deepest layer of the panniculus adiposus, in the designated localities. I usually inject a dose in each of the lower abdominal regions 3 to 4 cm. distant from Poupart's ligament, during the course of the constitutional treatment; in this manner a marked involution of the glands of the thigh and the inguinal region is at the same time effected.

Although the parts where the individual injections are made do not present a trace of change if these have been properly carried out,

I nevertheless also always choose the external lines of injection in place of those formerly selected in cases which necessitate renewed treatment with gray oil after a short time, let us say after months, on account of recurrent eruptions. I repeat that the skin should always be raised in a thick fold when injections are made, and the needle introduced deeply under the skin, and the cutis should not be pierced. Simple as this may seem, some skill is necessary nevertheless, and this is not possessed by all. The greater number of my pupils were able in a comparatively short time to make the injections in a perfect manner. Some were, however, so awkward that the injection was occasionally made too superficially, the cutis being pierced and the oil deposited in this. It stands to reason that after such an awkward injection, the reaction, which is usually slight, may go on to suppuration. It is not necessary, however, to make an incision in these cases, as the focus of softening occasionally becomes absorbed. But even should perforation occur, it will suffice to cover the spot with a plaster, as the thin pus soon ceases to flow, when the opening will close in a very short time. I repeat, nevertheless, that well-made injections will hardly ever lead to suppuration, and I feel justified in asserting that the seat of the injection will not suppurate, for the reason that out of the thousand injections which I have had occasion to make, certainly not more than two or three resulted in suppuration. Quite frequently even the patient will not be able after several, at the latest five to eight days, to designate the spot where the injection was made, and after the lapse of from eight to fourteen days the physician also is unable, as a rule, to discover a trace of the injection. The reason why subcutaneous injections of gray oil, made after my directions, do not leave any permanent changes behind is due partly to the small volume of the dose employed by me (0.05 c.c.). The doses recommended by others exceed in volume my own ten- or even twenty-fold (0.5 or 1.0 c.c.) and lead, as has been demonstrated, to destruction of the tissues, a marked inflammatory reaction, and later, even when suppuration does not occur, to hard, callous spots, such as are frequently met with in the gluteal region. The danger of the formation of a fat embolus, which is possible, is nearly always avoided, however, by using the small quantity just described, of the preparation to be injected. It stands to reason that after the subcutaneous injection of only 0.05 to 0.1 c.c. no destruction of tissue at all or only a very unimportant one is to be expected, while it may very well occur after the injection of 1.0 or even of 0.5 c.c.

Partly for this same reason, I avoid passing the needle into the glutei (maximus and medius) in a vertical direction. In making such

deep intramuscular injections into the nates, there is danger of puncturing one of the larger veins and emptying the contents of the syringe into it. Cases of pulmonary emboli, which I have, however, never seen, have usually, if not exclusively, been observed after injections into the glutei. On account of the comparatively limited area here, moreover, we run the risk of making the injections too close together or of injecting directly into a previous puncture, which may induce a reaction or even suppuration. At all events, hard callous foci will be formed which will prevent any further injections into the nates.

Although some physicians after making injections into the back have seen the formation of abscesses, I and many others have not had that experience, and the reason for this immunity is not to be found in the locality, but in the degree of skill with which the injections are made. Most persons are able to pass the needle vertically into the nates, and the manually skilful may also succeed in the application of a deep subcutaneous injection into the back at the first attempt, and even those possessing less dexterity will, doubtless after several unfortunate attempts, gain the necessary dexterity—especially to keep the needle in the loose cellular tissue and not to push it out again through the skin.

In selecting the back for the subcutaneous injections we also have the advantage of a large surface for the injections, which enables us to make as many of them as may be necessary. A large dose (for example 0.1 c.c.) may, sufficient room being present, be administered in two places (in doses of 0.05 c.c. each), and this is a very actual advantage in practice. It is fair to assume that when we inject a certain quantity of gray oil into a single locality we secure the absorption of less mercury than when the same quantity is distributed over two localities, and this supposition has been borne out by experiments. A. Kronfeld, for example, has demonstrated in experiments carried on in my clinic that a certain amount of mercury is much more rapidly absorbed if it is injected in two places than when in one. We may, therefore, assert with confidence that a large quantity of oleum cinereum injected in one spot is more slowly absorbed and therefore less immediately effective, while a more rapid absorption, therefore increased action, is obtained by the distribution of the same quantity in several localities. It is consequently much more advisable to inject small doses (0.05 c.c.), and to select the broad surface of the back as the place where they are to be made.

I have not had any extensive experience in the employment of subcutaneous injections in children and infants. I have, however, used the method experimentally in several cases and found it not only very effective but also well borne. For this purpose I employ

a twenty-per-cent. preparation (80) and inject partly into the back, partly on the external surface of the thigh in doses of 0.05 c.c. once or twice a week, that is, 0.01 gm. of metallic mercury at a dose. Moncorvo and Ferreira, who have a larger material at their disposal, made a number of experiments with various preparations for hypodermic injections, using for comparison calomel, yellow oxide of mercury, gray oil, salicylate of mercury, and corrosive sublimate, and express a very decided preference for gray oil.

Passing to the discussion of other points, I would emphasize the necessity of the physician being well informed as to the composition and the strength of the preparation which he injects. Thus, some simply prescribe "oleum cinereum" when they wish to make injections, without any further description; but as gray oil, like every other preparation, may be made of various degrees of strength, a prescription of this kind is as unsatisfactory as would be the ordering of powders of opium or morphine, without making mention at the same time of the quantity of opium or morphine which these should contain. The difference, moreover, is very great, for the reason, as has been mentioned, that a dose of 0.05 c.c. of the fifty-per-cent. preparation of gray oil contains 0.04 gm. of metallic mercury, while the same volume of a thirty and twenty per cent. preparation contains one-half or one-fourth the proportion of mercury.

Under the use of this gray oil the syphilitic products as a rule disappear positively and symmetrically, and the effect on the disease is quite permanent. Aside from this, we note polyuria and increased appetite in many patients, also an increased metabolism which quite frequently finds an expression in increase of bodily weight.

In addition to gray oil very many insoluble or imperfectly soluble mercurial preparations have been employed. These are also of great value in certain cases and call for brief mention. As a rule they are prescribed in suspension, in the proportion of 1 gm. of the mercurial preparations to 10 gm. of oil, and are injected in the dose of 1 c.c. of the mixture. This practice is in my opinion a pernicious one. These suspensions, as above noted, do not allow of an exact dosage. H. Krause had an unpleasant experience, in that a patient who was the last of a series to receive injections of calomel showed symptoms of poisoning, and this was doubtless due to the fact that the drug had sunk to the bottom of the mixture and so was given in much larger doses than was intended. Aside from this, there are other grave objections to the use of these drugs in suspension. The proportion of metallic mercury in the different preparations in equal quantities by weight is very variable. If, for example, I inject half a syringeful of calomel or oxide of mercury in suspension, in the pro-

portion of one to ten of oil, I introduce more metal into the body than is contained in the same quantity, in a similar suspension, of thymolate or salicylate of mercury. To avoid this inconvenience, I have had the other insoluble or slightly soluble preparations of mercury also prepared with lanolin and oil in such proportions that a mixture is formed similar in strength to the gray oil, and which, like it, is solid at ordinary temperatures, and must therefore be slightly warmed before it is injected. The active constituents, therefore, remain more equally distributed, and can be more exactly dosed than is the case with ordinary suspensions. I have in this manner obtained preparations of thymolate of mercury (85), salicylate of mercury (83), yellow oxide (82), black oxide (84), calomel (81), and bicarbonate of mercury (86), which contain respectively 0.36, 0.42, 0.39, 0.39, 0.37, and 0.36 gm. of mercury in each cubic centimetre. Thus, according to the rules given for oleum cinereum, they may be used for injections in the treatment of constitutional lues, in doses of 0.1 c.c.—like the thirty-per-cent. gray oil. These mercurial salts should be finely powdered, and carefully triturated with the lanolin and oil. The preparations mentioned necessitate needles with a larger bore, while for a carefully prepared gray oil very fine needles may be used.

For the injection of these preparations, also, I prefer the back. Reported instances of embolic pulmonary infarcts have occurred in cases in which the suspended preparations were injected into vessels. Cases have been observed of a violent, long-continued cough, cyanosis, and pain in the back following an injection of mercury suspended in oil, especially of the tannate, the yellow oxide, and the salicylate; more than that, even slight dulness, crepitant râles, and a rough expiratory murmur have been noted. These symptoms, as a rule, disappear again in a few days. In my experience pulmonary emboli may be avoided if the preparations are made as above directed, that is to say, if the proportion of fat is reduced and the injections are invariably made in the back.

The reaction mentioned above in the discussion of gray oil which is accompanied by a rise of temperature after the first injection, has also been observed with the other preparations and is somewhat more intense in these cases than when gray-oil injections are used.

The mercurial preparations above enumerated have a powerful action on the syphilitic process, and it may even be said that in certain cases of their employment involution runs an acute course—a precipitate one, if the expression may be used, and it almost always occurs more rapidly than when other methods of treatment are employed. According to the expression of H. Leloir, the syphilides dis-

appear with a "véritable brutalité" after calomel injections. Jullien is also a warm advocate of calomel. With all this recognition of the excellence of the preparations mentioned, I must, however, confess that relapses in many cases occur earlier and in graver form, as my experience has taught me, than after other methods of treatment. We shall recur to this later.

Of the *soluble salts of mercury*, corrosive sublimate for a long time was used for subcutaneous injections, usually in the form of a one-per-cent. aqueous solution. In the course of time, however, the mode of preparation of this salt has undergone various changes. At the present time the bichloride of mercury dissolved in a solution of common salt (88) is universally employed. One to two cubic centimetres of this solution, representing 0.01 to 0.02 gm. of corrosive sublimate, is injected daily or every other day. Corrosive chloride of mercury may also be employed in a more concentrated form, but in that case the injections will, of course, have to be made more infrequently. W. Lukasiewicz increased the concentration to 0.5 per cent. and George J. Müller to 0.8 per cent., 1 c.c. of this solution being injected once a week. In my experience a 0.3-per-cent. solution of corrosive sublimate (89), injected every third or fourth day, has an excellent effect. The reaction and tenderness will be the greater, as may be surmised, the stronger the solution; but injections of this strength are, nevertheless, on the whole, well borne.

A number of organic mercurial preparations (cyanide, glycocoll, formamide) which do not precipitate albumin have been recommended for subcutaneous injections. The glycocoll and formamide (90) injected daily or every other day in one or two per cent. solution, are classed with the milder but nevertheless well-acting preparations. I have also found the succinate of mercury useful; it is injected, as advised by A. Wolff, with the addition of a slight amount of cocaine (91), like all the other soluble preparations, in the form of a one-per-cent. solution. The sozoiodol is a preparation recommended for injection of the rapid action of which I have repeatedly convinced myself. It is retained in solution by the addition of iodide of potassium, and is injected in a concentrated form (87) once a week.

This by no means exhausts the list of mercurial salts which have been recommended for subcutaneous injection, but we have limited ourselves to a consideration of the preparations that are most frequently used.

We shall do well, when employing the soluble mercurial preparations, also to observe a certain order in the injections. It is advisable to inject the first dose on both sides of the spinal column, and the subsequent ones below in a series forming two parallel lines. In

this way we are able to divide evenly a large absorption area into many smaller regions.

We ought, however, in employing subcutaneous solutions, to inject a small portion in the neighborhood of the most intensely affected parts. The pain which is caused by the injection varies according to the kind and strength of the solution used, but is bearable, even after the use of concentrated solutions, and does not last long. In individual cases, however, we shall find the patient so sensitive as to force us to abandon the method. There is scarcely any preparation that does not produce some reaction. A firm, more or less painful infiltration is produced at the place of injection, which is occasionally absorbed within a few days, but occasionally remains much longer. Suppuration rarely occurs. Formamide of mercury, besides producing the least constitutional effects, also produces the mildest local reaction. The other preparations, if used in like concentration, do not seem to differ greatly from each other as regards the symptoms of reaction. Yet even here great individual differences are to be noted.

We may mention still another method of injection in which the mercury enters the blood directly. This method was introduced by Guido Baccelli, of Rome, and consists in injecting the preparation (corrosive sublimate) directly into the veins, thus practising an *intravenous injection* of corrosive sublimate. The veins at the periphery of the arm or leg are made to swell by pressure of the finger or a bandage; the skin of the previously disinfected area is then made tense by the application of two fingers, one on each side of the vein, and the needle (which must be sharp and aseptic), attached to the filled syringe, is plunged through the skin and wall of the vein. Pressure is made on the piston and a small portion of the contents of the syringe is expressed; if the skin does not now bulge out, the needle is in the lumen of the vein. Compression is now removed from the vessel, all the fluid contained in the syringe is injected into the vein, the needle is removed, and the puncture is covered with a piece of iodoform gauze, which is painted with a small quantity of iodoform collodion. If the injection has been well made, the skin, as already observed, should not puff out, nor should pain be experienced; both take place if the injection has been made subcutaneously instead of intravenously. Solutions of 0.1 to 0.2 per cent. strength are used, and of these 1 c.c., representing 1 or 2 mgm. (gr. $\frac{1}{6^{0}}-\frac{1}{3^{0}}$) of corrosive sublimate, is injected. If it is found necessary we may gradually increase the dose up to 8 mgm. a day, and may, in grave cases, begin at once with 4 to 5 mgm. in a 0.2-per-cent. solution. Blaschko has increased the dose to a 0.6-per-cent. solution.

The advantages of this procedure are obvious. By the direct introduction of mercury into the blood the remedy reaches the diseased area by the shortest route, while in all other modes of application this is possible only through the medium of the chylous or lymphatic apparatus. In spite of the small amount which is injected intravenously, the action of mercury is at once very distinctly apparent, as the patient experiences a salty taste a few minutes after the injection and soon after a metallic taste, and may even become salivated within five or six minutes (Baccelli). The mercury makes its appearance also in the urine within an hour after the injection, but disappears again on the following day. When the injections are repeated daily, the excretion of mercury is, of course, a continuous one. It may occasionally continue for a week after the last injection, but in no case could mercury be found in the urine after two weeks (A. Blaschko).

The greatest advantage of this method lies in the direct introduction of mercury into the blood. Although the syphilitic virus, as we have previously observed, is doubtless a tissue parasite, we must also bear in mind that certain poisonous products of its metabolism, toxins, circulate in the blood, and are here most readily attacked. The benefit to be obtained in cases of arteritis syphilitica is, of course, much greater, for the reason that the medicine when intravenously injected is taken up by the blood and brought directly into contact with the diseased vessels. Inasmuch as syphilitic affections of the brain are very frequently due to arterial disease, this method would seem to be indicated most urgently in cerebral lues; the drug may, however, be directly and consequently most rapidly brought into contact with other syphilitic intracranial lesions when introduced in this way.

There are, however, certain inconveniences in this method which prevent its general application. Although a well-made intravenous injection does not cause pain or swelling, an infiltration at a certain part of the vein will usually form within the next few days, as I have repeatedly observed, and will remain stationary for some time. As new localities are chosen for the subsequent injections, the number of points of infiltration will of course increase, and when the treatment is of long duration we shall finally be embarrassed to discover any portion which has remained intact, and which would be suitable for the intravenous injection; we shall, therefore, be forced to discontinue the method and complete the cure in some other manner. In addition to this, as M. Dinkler has demonstrated clinically and experimentally, thrombotic deposits appear within a few days on the wall of the vessel, and may, in case the

treatment is not interrupted, lead to a total obliteration of the lumen of the vein.

We might, as I have advised, employ *paravenous* instead of intravenous injections. In this method stronger solutions of corrosive sublimate (as high as one per cent.) are used, of which 1 c.c. is injected subcutaneously alongside of the vein. The mercury, by diffusion, rapidly enters the passing blood current, and in this manner we are able in a short time to introduce larger quantities of the preparation into the circulation than we could hope to do with the usual subcutaneous injections in which the mercury is taken up by the lymphatics. Further and comparative experiments with the intravenous and paravenous methods of injection are greatly to be desired.

The digestive tract is also very suitable for the reception of mercurial preparations. We must only have a care that in their ingestion no direct irritation of the gastroenteric canal or symptoms of acute mercurial intoxication (see below) are excited.

Metallic mercury is best dispensed in the form of blue pills (92). Tannate of mercury (93 to 95), introduced by Sigmund Lustgarten, is a very active preparation; it should not be administered, however, with the alkaline carbonates or iodine preparations. Calomel is administered in the form of powder or pills (96 to 99), and corrosive sublimate may be given either in the form of pills or in an aqueous or alcoholic solution (101 to 104). Protoiodide of mercury is also a very useful preparation (100).

On account of the greater ease of administration the mercurial preparations are preferably given in the pill form; in this case we should remember, however, that old pills (those which have aged either in the pill box of the patient or on the shelves of the apothecary) frequently dry to such a stony hardness that they are not dissolved by the intestinal secretions, and pass off unchanged in the fæces like shot. The careful physician will therefore impress on his patients the necessity of using only freshly prepared pills. We should remember, however, that some patients will, in spite of this warning, use up their old supplies. To avoid this annoyance I use a pill mass which will dissolve at the temperature of the body. This is described in the formula (No. 92) for my gray pills, which are made of mercury, lanolin, and sugar of milk; as the lanolin and sugar of milk dissolve in the economy, the mercury which is released is readily absorbed. A similar pill mass is employed as an excipient for the protoiodide, the tannate, calomel, corrosive sublimate, etc.

Mercurial preparations administered by the mouth should be given immediately after meals, as they would otherwise create dis-

turbance in the stomach and the intestines. Occasionally diarrhœa will make its appearance in spite of this precaution, but so long as only two or three stools of moderate size, unaccompanied by much pain, are passed in the twenty-four hours, the medicine need not be discontinued. Should the evacuations, however, become more frequent and be accompanied by pain in the abdomen, a dose of opium should be administered at the same time with the mercury. Should the diarrhœa persist, the internal administration of the mercurial must be discontinued. When corrosive sublimate is taken, the accompanying symptoms on the part of the intestinal canal should receive special attention.

If the intestinal tract proves tolerant, very favorable results may be obtained by internal medication, but we must not overlook the fact that on account of the small quantity of mercury which can be introduced in this manner (large quantities will absolutely not be tolerated for any length of time), the treatment will have to be continued for a very long time, with occasional interruptions. In the case of inunction or injection, as we have seen, there is a deposit in the tissues which can be drawn upon gradually, but there is none such when the drug is given by the stomach, and this defect must be supplied by a long-continued treatment. In any case, very powerful effects are not to be obtained with internal medication.

No matter by which method mercury is introduced into the organism, it always enters the fluids of the body and is expelled in secretions and excretions, as has been shown by numerous experiments made with great care by many authors. The mercury reaches all the tissues through the circulation, although it is not found equally distributed. The researches of E. Ludwig and E. Zillner, as well as the experiments of K. Ullmann and J. Pal, have given us most detailed information as to the distribution of the mercury in the animal economy. The greatest amount of mercury can be found in the kidney, next in the liver (the bile, however, containing only a small percentage); the intestine and spleen contain large quantities of the metal, the thymus gland not so much; while the bones, muscles, brain, and lungs contain only small quantities of mercury. The presence of mercury in the blood is of great importance; Welander is said to have found it abundantly there. After the application of mercurial ointment he was able to demonstrate the presence of the drug in the pus of an abscess; it was also found in the placenta, blood, liver, and urine of the fœtus as well as in the mother's milk, after the latter had been treated with mercury. It is eliminated by the secretions and excretions; thus it has been detected in the saliva, the sweat, the bile, and the milk. It is excreted in greatest amount

in the urine and fæces; the urine contains mercury within one or two days, sometimes even a few hours after its first exhibition. More mercury is found in the urine after subcutaneous injections and inunctions than after any other way of introduction.

I long since convinced myself by direct clinical experiment that mercury administered in large laxative doses is absorbed to a great extent. A colleague suffering from grave syphilis was under the impression that he could best cure a stubborn constipation by a large dose of calomel. The effect was all that could be desired; he was, however, affected for a number of weeks by a stomatitis mercurialis, although he had not taken any mercury for several months previously. A. Wolf and J. Nega have, moreover, demonstrated by direct experiments that for thirteen days after the exhibition of calomel in laxative doses mercury may still be found in the urine. Welander found it present within four hours after a laxative dose of 0.6 gm. (gr. x.) calomel, and was able to demonstrate its presence in the urine during the following eighteen days. In a case in which calomel was repeatedly administered for diuretic purposes Pal was able, twenty-five days after the last dose, to demonstrate the presence of 0.3 mgm. of mercury in 300 gm. of urine passed in twenty-four hours. Mercury has also been found in the urine after the application of my mercurial plaster, and after gray rectal suppositories.

The excretion of mercury in the urine, in spite of the statements of earlier authors, is constant and follows the rule that the quantity increases during treatment and gradually decreases when the treatment is discontinued. A certain amount of mercury is, however, retained in the system. Landsberg was able to demonstrate its presence ten months, and Welander from six to twelve months, and even longer after treatment had been discontinued. In two of my own patients it could be demonstrated seventeen and twenty-three months after the last injection of gray oil, and in two others three and ten years after the last course of inunctions. Two of these patients were nearly continuously under my observation, and the other two examined for this purpose had kept careful record of their cases from the time of infection, so that the statements as to the periods following treatment seem reliable enough. Mercury when applied by inunction, and especially when injected, is undoubtedly retained in the tissues for a long time. Mercury taken into the system by internal medication is also certainly found in the urine some weeks after treatment, but its period of retention in such cases bears no comparison with that following the endermic or the hypodermic application of the remedy.

To return to the constitutional treatment by mercury, we must

be well acquainted with the energy of action, indications, and contraindications of the various methods of treatment and preparations, so as to be able to compare their value one with the other. Subcutaneous injections belong to the most effective therapeutic methods, but symptoms of poisoning (see below) are probably more frequent after this procedure than after any other mode of exhibition of the drug. Among the mercurial preparations used for subcutaneous injection the insoluble or slightly soluble are more effective than the soluble. As regards the former they also differ among themselves, in so far as injections of calomel, of thymolate or salicylate of mercury, and perhaps also of oxide of mercury, act much more rapidly on the syphilitic process than gray oil; on the other hand, relapses are much more frequent than when the latter remedy is used. Whoever has used oleum cinereum very extensively and become acquainted with its employment, cannot but become convinced of its favorable action. As to the infrequency of relapses after oleum cinereum other observers have had experiences which correspond with my own. In Leichtenstern's clinic especially, where the whole material of prostitution of the city of Cologne is aggregated, nearly the same results have been noted. That excellent results may also be obtained in cerebral syphilis with gray oil is recorded by J. Sacaze and E. Magnol from the medical clinic at Montpellier. Georges Thibièrge, who experimented with gray oil in Besnier's clinic, while not favoring the exclusive employment of this preparation, especially emphasizes its great value. Besnier reports a case in which relapses occurred again and again in spite of treatment extending over fifteen years, in which a cure was finally and permanently effected by the employment of oleum cinereum. L. Le Pileur, after a large experience with gray oil, believes that its employment is indicated in the majority of cases of syphilis. Even Fournier, who prefers internal treatment to any other method, can find only words of praise in favor of gray oil. Its application, he says, is not at all painful, at least not in the same measure as calomel, and he adds that even though injections of oleum cinereum do not act so rapidly as calomel injections, they still act rapidly enough in the majority of cases. He mentions also the permanency of the results obtained with gray oil. My own experience in the use of gray oil covers a period of fourteen years. So far as I may be permitted after such a period of time to judge, I can say that I have met with unusually satisfactory results in a very great number of cases. The most convincing observations were of patients in private practice, as I was able to observe most of them for years; among them there are quite a number of physicians who had themselves contracted the disease. Many patients underwent only one course

of injections with gray oil, but in some cases the occurrence of slight relapses necessitated at the end of six months or a year from four to six injections of 0.05 c.c. of the fifty-per-cent., or 0.1 c.c. of the thirty-per-cent. solution of oleum cinereum. The cure after this second course was definitive. The permanency and the actuality of the cure was evidenced in many cases by the fact that the patient married and no trace of syphilis ever appeared in either wife or children. These patients married with my consent, given after careful and repeated examinations. But there were a few others who, under the pressure of circumstances, but against my distinct orders, married a few months after having completed a course of injections, and still the wife and children remained healthy.

In isolated cases relapses have occurred in later years, but severe forms I have seen only very exceptionally. The most positive proof of the final cure of syphilis we find in reinfection. I have records of seven such observations among my patients treated with gray oil; of these five belonged to my private practice and only two were seen in hospital. Hospital patients, on the whole, are less favorable for the observation of the therapeutic effects of a remedy. Aside from the fact that most of them lack the intelligence or the opportunity to live according to the absolute dictates of hygiene after leaving the hospital, many wander from one hospital to another, or else they are lost sight of altogether. In spite of all this, however, only very few cases recur to my mind in which the relapses were of grave form; as a rule they appeared as slight irritative cutaneous and mucous-membrane eruptions.

I am well aware of the fact that similar favorable results are also claimed for other methods of treatment, provided they have been properly carried out, but feel justified in the statement that gray oil in this respect is far superior to other methods of application, at all events it is not inferior to them.

As regards the soluble preparations of mercury, very prompt results are obtained from their injection, but with the more concentrated preparations we note a more rapid, so to speak, precipitous action in comparison with that following the daily injection of milder solutions.

It is an interesting fact that injections of a concentrated solution of corrosive sublimate are followed by alterations in the blood, namely, a primary thickening and a consecutive thinning, while after inunctions or injections of gray oil the specific gravity of the blood remains unchanged (H. Schlesinger).

Smearing with blue ointment and the use of mercurial soaps, or of resorbin with mercury, come next to the inunctions and injections,

as regards the intensity with which they influence the syphilitic process. The plaster treatment and the use of electric corrosive sublimate baths should also be classed with the effective methods of treatment.

In grave cases, the internal administration of mercurial preparations is least to be relied on, as the intestinal canal is injuriously affected by even medium doses in many cases, and almost certainly by larger ones. Nevertheless, we are frequently able to obtain very good results in affections of a medium and slight degree by the internal use of mercury; it is necessary, however, to administer the drug, although in small doses, during a comparatively long period of time.

In accordance with our general experience, we may therefore say that although individual methods of treatment vary greatly in their effect, we may, nevertheless, make use of each one of them successfully; it is, however, necessary as a fundamental condition that the physician be intimately acquainted with the individual methods of application.

Should, in a given case, the conditions be such that no contraindications are present to the use of either of the methods, we would naturally choose that which presents the greatest advantages. There is at present no question that the subcutaneous injections, carried out according to the rules above laid down, so far as the precision of dosage and certainty of effects are concerned should be placed in the foremost rank. This method also possesses the great advantage that it may be employed in the case of outdoor patients with greater certainty of results than any other method.

In the order of preference, to recapitulate, we have subcutaneous injections of gray oil, calomel, thymolate and salicylate of mercury, and in the second rank injections of soluble mercurial preparations; next in order are inunctions, smearing, the use of mercurial soaps, plaster treatment, and electrical corrosive-sublimate baths; and finally, internal treatment. We are, however, quite frequently limited in our choice by the necessity of selecting a method which will adapt itself to the external circumstances of the patient. In ordinary cases we cannot adopt any method indiscriminately with certainty of success, but we must decide in favor of one or another method according to the indications present. The method selected in the beginning may frequently, when no contraindications occur during the course of the disease, be continued to the end. In other cases again we are confined to some distinct method of application; the practical physician should, therefore, endeavor to become familiar with them all.

Assuming that we have to deal with a grave case of syphilis of

the brain, of the eye, or of the respiratory passages, which on account of the immediate danger necessitates a rapid cure, say a rapid absorption of the threatening focus, the indication will be to begin with a few (two or three) injections of calomel (81), thymolate of mercury (85), salicylate of mercury (83), or oxide of mercury (82), or one or another of the strong solutions of mercury (89), and to continue the treatment with gray oil (78) or inunctions (75).

In those difficult cases in which we wish to arrive at a diagnosis ex juvantibus, injections of insoluble preparations of mercury, especially gray oil or calomel, or of sublimate are best employed. A few doses subcutaneously will enable us to arrive at a decision more rapidly than when other mercurials are used. On the other hand, debilitated patients, who are naturally hypersensitive, or whose skin is covered with painful nodes, are best treated by smearing the ointment on the skin, or under certain circumstances with mercurial plaster; and later, when they have grown somewhat stronger, with electric baths or subcutaneous injections.

Patients suffering with extensive ulcerations are very favorably influenced by corrosive-sublimate baths, but also by smearing or the application of mercurial plaster; after the ulcerations have diminished in number or healed, injections or inunctions may be resorted to.

Pregnant women bear injections of gray oil, inunctions, and also smearing very well; it is not, however, judicious to administer mercury to them per os. It will only rarely be necessary to interrupt mercurial treatment on account of menstruation.

We occasionally find patients who are restricted to internal medication, as they are unable, from certain obligations imposed by their station in life, either to carry out a cutaneous treatment or to pay regular visits to the physician in order to receive injections. Many conditions may arise, moreover, which compel the physician of necessity to be conversant with different methods. Individual patients are so sensitive to each puncture of the needle, without any obvious cause, that this method will have to be abandoned and some other method pursued. Others, though this is very exceptional, react to every attempt at inunction with an acute erythema; naturally in such a case another method will have to be followed. Still others show a special intolerance of the digestive tract for mercury, internally administered, and in these the indication is undeniably for some other method of application; or the stomach must be protected for the reason that internal treatment is perhaps at the same time pressingly indicated for some complications.

When shall we begin temporary constitutional treatment? Leav-

ing out of consideration the stage of syphilis between the appearance of the initial lesion and the first constitutional symptoms, the general treatment should begin at once.

When we are dealing with a recent initial lesion, the possibility of preventive treatment may be considered. If the initial lesion has already existed for some time, so that constitutional symptoms are to be expected in the near future, it is well quietly to await their full appearance, and then only to begin constitutional treatment. But we also see cases in which the initial lesion runs an unusually protracted course, by reason most probably of ulceration, which progresses constantly in spite of scientific local treatment. The affection then loses the characteristics of the initial lesion, and occasionally presents the form of a later product of syphilis, that of a serpiginous ulcerative gumma; occasionally it appears, and this is a worse case, as though the syphilitic infiltration accompanied by degeneration extended along the lymphatics. In such a case it may be that in spite of the originally very marked initial sclerosis, signs of the constitutional affection are occasionally delayed for an unusually long period.

In initial lesions of this kind I prefer to rely on local surgical treatment (see above); but if the lesions cannot be removed by a radical local treatment, as for example in cases in which the morbid infiltration extends into cavernous tissue and the radical removal of the diseased parts would lead to marked deformity, I then resort to constitutional treatment, especially if the stubborn course of the initial sclerosis just described is of unusually long duration, even though no signs whatever of a constitutional affection are present, and this very rarely fails to exert a favorable influence on such an initial lesion.

In other cases again the initial lesion will go on to a normal cure under the usual treatment, but after sufficient time has elapsed for the appearance of the constitutional symptoms the patient becomes anæmic and complains of continued or periodical headache, rheumatoid symptoms, and general discomfort, while an objective examination either does not reveal any morbid changes at all, or only a few, such as three or four lesions in the palm of the hand or on some other part of the body. In these cases, also, I feel justified, in spite of the absence of manifest constitutional symptoms or their presence in incomplete or indistinct form, to initiate an energetic constitutional treatment; and this especially if the symptoms mentioned continue for a long period and thereby justify the suspicion that the generalization of the virus has led to irritative processes in the deeper or vital parts, such as the nervous system, muscles or their sheaths, etc., instead of affecting as usual the skin or mucous membranes.

The treatment, when first applied, should be thorough. Affections of the central nervous system, the organs of special sense, the peripheral nerves, and the viscera, as well as gummatous affections in various localities are, as will be explained later on, quite frequently influenced most favorably by the compounds of iodine; but for a radical cure an energetic mercurial treatment is generally absolutely necessary. Consequently not only the first constitutional symptoms, but also every following severe syphilitic attack should be treated most thoroughly according to the rules above discussed. In early relapses, on the other hand, from four to eight injections of gray oil, or twelve to twenty inunctions or paintings usually suffice. We are frequently obliged to subject individuals to a full mercurial course who do not present the slightest symptoms of lues, but who nevertheless have what I would call transferred metaphoric symptoms. If a person has acquired syphilis years ago, which was seemingly cured after, let us say, a scientific treatment, and we then discover that his children are affected with hereditary syphilis, we are obliged, on the ground of this metaphoric symptom, to administer a thorough mercurial and perhaps also iodine course to both parents. I do not hesitate also to administer to previously infected individuals a mercurial course under all circumstances before they contract a marriage. This treatment may be in the form of eight to twelve injections (on the whole about 0.4–0.6 c.c.) of the fifty-per-cent. solution of gray oil, and also of iodine; this I do even when sufficient treatment has been given previously and observation for some time has not revealed any symptoms of disease.

Preventive Treatment.

For a number of years I have methodically carried out a method of preventive treatment; the number of patients has been quite large, and I have become convinced that we are here dealing with an important therapeutic principle. I apply preventive treatment in all cases of recent initial lesions, where excision or abortive treatment is insufficient or impossible.

For the preventive treatment I find it sufficient during the first two months to inject every five to eight days one dose (0.05 c.c.) of a fifty-per-cent. solution of oleum cinereum. The first two injections, when the lymphadenopathy is not of an inflammatory nature, I make deeply under the skin on the right and left side of the abdomen, three finger breadths above Poupart's ligament, so as to act upon the inguinal glands; the others are made in the back as usual. After the first two months have passed, the same dose is administered at intervals of ten to fourteen days. Altogether from twelve to sixteen

doses, 0.6–0.8 c.c. of the fifty-per-cent. solution of gray oil are given.

When treatment has been carried out in this manner an obvious influence is exerted on the syphilitic process. Not only do the initial lesion and the lymphadenitis retrograde, but in some cases the constitutional disease fails to make its appearance, and in many, probably in most cases, the general character of the syphilis is modified, rendered milder, the constitutional effects being delayed and the eruption being scanty and in the form of isolated erosions in the mouth or fissure-like plaques on the tonsils; or a few, large, dull maculæ or circles or a very few pale scaly papules, occasionally joined in groups, show themselves on the skin. The patient remains under observation for a certain period, and if symptoms of syphilis occur, a few doses of gray oil are frequently sufficient to cause their disappearance.

If we wish to employ other methods of treatment for prevention, they will have to be used in a similarly modified form. Inunctions as well as smearings are to be made every other day at first, then twice and once a week, etc. If we are confined to internal medication, from three to five gray pills a day, for example, may be administered in the beginning, later one to three a day are given; other mercurial preparations would have to be employed in proportionate doses.

Mercurial Poisoning.

No matter in what manner the mercury is incorporated into the system, we must always be prepared to see at any time a series of symptoms caused by the presence of this metal which are by no means indifferent, and which together make up the condition known as *hydrargyrosis* or *mercurialism*.

We shall first describe briefly *chronic mercurial poisoning*, as it appears in certain trades, such as quicksilver mining, hat-making, mirror-making, etc. Disturbances of digestion are usually the first symptoms presented, being caused by a catarrh of the stomach and intestines; now and then an increased secretion of saliva and stomatitis are noted, and following this symptoms of anæmia and increased irritability occur. The patient is easily frightened, becomes embarrassed and confused by the slightest causes, and seems awkward and clumsy, especially when he thinks himself observed; his sleep is restless and disturbed by dreams. In the further course of the intoxication a tremor is observed, which begins in the facial muscles and the tongue, extending to the extremities, and may increase to convulsions; during sleep the tremors cease or at least become much dimin-

ished. Paralysis then succeeds the tremors if they are very marked. Neuralgias also in the form of pains in the extremities, oppression of the chest, and especially headache and toothache make themselves felt in the most troublesome manner. Loss of intelligence is not so very infrequent, but actual mental disturbances only exceptionally occur. If the cause has been in action for a long time, a *mercurial cachexia* is induced during the long continuance of these conditions. In the course of this cachexia the bones become fragile; pulmonary phthisis is frequently developed; occasionally albuminuria of a short duration occurs, nephritis not necessarily being present; dropsies are terminal symptoms in grave cases. Women in this condition are very liable to abort, and the children who are born of them are weakly and debilitated and frequently become the victims of scrofula or rickets.

The other extreme of hydrargyrosis is represented by *acute mercurial poisoning*, in which gastroenteritis, even in the fatal cases, is the most prominent symptom.

The therapeutic use of mercury also induces certain forms of acute and chronic hydrargyrosis, which the physician ought to be able to recognize distinctly. The pathological changes caused by mercury occur singly or in groups in the oral cavity, the intestines, and the kidneys. In addition to these typical locations, the evidences of poisoning not very infrequently exist in the skin, and we may also occasionally note the creation of a hemorrhagic diathesis and certain more or less grave disturbances within the sphere of the nervous system.

The abuse of mercury, no matter what preparation is employed or in what manner it is applied, may result in such grave disturbances that death directly results. Mercurial treatment may also, as we shall see later on, greatly endanger life in consequence of the induced cachexia, or in other cases an idiosyncrasy exists, with the nature of which we are not as yet very well acquainted. It is therefore absolutely necessary to comprehend thoroughly all the conditions which may arise during the treatment of syphilis with mercurial preparations.

The first symptom of mercurialization which presents itself in the course of the therapeutic use of mercury is quite frequently a *metallic taste* in the mouth, the patient complaining of a sensation as though he held a copper coin or a key in his mouth. At the same time an increased excretion of saliva is noticed—ptyalism, *salivation*—occasionally to such a degree that the patient is greatly annoyed by the continued dribbling from the mouth. This is accompanied by inflammatory swelling of the gums, especially of the lower jaw (*gingivitis*).

The gingival pyramids between the front teeth are red, swollen, and covered with a purulent deposit; occasionally the mucous membrane of the hard palate, immediately behind the incisors, is affected, or the process bears mainly on the gum about the posterior molars so that it frequently covers the crowns of those teeth. The same process may also involve the tongue and cheek in case the mercurialism increases, and even the tonsils—in short, the whole inside of the oral cavity (*stomatitis mercurialis*). When the swelling is marked the indentations of the teeth are seen on the borders of the tongue and on the mucous membrane of the cheek, leading here sometimes even to ulceration. In other localities we often find superficial ulcers of the mucous membrane covered with a dirty deposit and surrounded by a red border (*mercurial ulcers*); at the same time there is a disgusting *odor* issuing from the oral cavity. In still graver cases, as a rule, those that have been neglected or in which large doses of mercury have been mistakenly given, the inflammatory process extends to the periosteum of the alveoli, which becomes swollen and so presses the teeth out of their sockets; the teeth, indeed, appear to the patient to be elongated, they are painful and loose, and occasionally fall out. The periostitis of the alveoli may even extend to the maxilla and cause necrosis, and the inflammatory swelling of the soft parts may also lead to extensive gangrene. However, if the case is carefully watched any grave injury from medicinal hydrargyrosis will hardly occur, as the proper treatment can be instituted at the appearance of the first symptoms of mercurialization.

The oral affection just described appears occasionally after small doses of mercury, as a rule, therefore, during mercurial treatment; but cases are also met with in which salivation occurs some time, from one to four weeks, after treatment has ceased. Louis Jullien and others have noted the occurrence of salivation one or two months and even much longer after the discontinuance of the mercury, in whatever form the drug may have been given.

Occasionally the first symptoms of hydrargyrosis present themselves in the region of the *digestive tract;* the stomach and intestines are then affected by catarrhal conditions; digestion is disturbed, colicky pains are felt, the stools become more frequent, watery, and occasionally bloody, and even grave dysenteric conditions may develop (mercurial enteritis, colitis, or dysentery). The digestive tract, as the chief emunctory for the excretion of the mercury, is liable to be affected no matter what may have been the mode of administration of the drug. The stomach, furthermore, has a great affinity for the mercury circulating in the blood, so that dyspepsia and gastrectasia (Jullien) may follow a mercurial treatment. I have observed

two cases of grave dyspepsia which were obviously induced by antecedent mercurial inunctions.

The influence of mercury on the *kidneys* has already been referred to, and it will therefore suffice to mention albuminuria and cylindruria which may follow the use of mercury, however it may be administered. In my own experience, which coincides with that of Welander, we are dealing here, excluding cases of actual abuse of mercury, with a purely temporary symptom, which is not accompanied by any detrimental results to the organ.

We may mention, in addition to the cardinal symptoms of medicinal mercurialization just discussed (salivation, enteritis, albuminuria), certain other less frequently observed but not less important symptoms of intoxication.

Changes in the *nervous system* as well as in the voluntary and involuntary muscular apparatus are among the effects of mercurial poisoning. These in their lighter forms cause restless sleep and rheumatic pains in the extremities. It is, however, of the greatest interest to note that acute hydrargyrosis may also lead to grave changes in the nervous system, to an actual *polyneuritis*.

One of the less frequent symptoms of medicinal hydrargyrosis is a *toxic erythema*. We have already mentioned, in speaking of inunctions, that these may cause in exceptional cases severe exudative changes, which should by no means be looked upon only as a local effect of mercury, but rather as the expression of a general toxic disease of the skin. Similar cutaneous affections have also been observed following the internal as well as the subcutaneous use of mercury. We find acute punctiform, discoid, or oval patches of erythema which are occasionally raised in the form of a wheal, or arranged in gyri, in debilitated, anæmic persons. There may be points of ecchymosis the size of a pinhead, or vibices, some coinciding with the erythematous lesions, others located in otherwise normal areas of the skin; small ecchymoses of this kind are more frequently met with on the legs. Again, in other cases the eruption is intense and takes on a deep scarlet color. Corresponding to the degree of exudation we find blisters and later copious desquamation; I have even observed an acute eruption of pemphigus-like lesions. If the mucous membrane of the oral cavity is involved, which may also occur, we might mistake the affection for a common mercurial stomatitis. The erythema is occasionally accompanied by fever, and the patient feels weak and depressed. As a general rule, the affection runs its course in a few days, and desquamation generally occurs at the end of the process.

Fortunately this medicinal hydrargyrosis, if treatment is prop-

erly carried out, occurs only in a small percentage of patients treated with mercury. All patients, undoubtedly, do not react to mercury in the same manner, but we are altogether in the dark as to why some patients bear comparatively large doses of mercury while others are affected injuriously by small quantities.

In certain pathological conditions, it is true, intolerance of mercury occurs more readily, yet I have frequently found patients suffering from the same defects who bore mercury very well. It will be well, however, to discuss this subject somewhat at length, since we may thereby gain some important information which will be of service in our treatment of syphilitic patients. A bad condition of the *teeth* may unfavorably complicate the mercurial treatment. Carious teeth, broken crowns, retained stumps of roots frequently make possible the entrance and growth of pathogenic germs which, even when there is only a slight swelling of the mucous membrane and loosening of the epithelium, find a congenial soil to excite and maintain inflammation. Should stomatitis mercurialis at the same time occur, it will naturally assume a grave form, being added to a local injury already present.

The situation is still more unpleasant if affections of the *stomach* and *intestinal canal* are already present. The internal administration of mercury in such a case acts directly as an irritant; but even the cutaneous or subcutaneous employment of mercury may also act unfavorably on the digestive tract, for the reason that, as we know, the intestinal canal is one of the most important organs for the excretion of mercury.

Affections of the *kidneys* are no less dangerous as predisposing to or aggravating mercurial poisoning. From the fact that the kidney plays a very important rôle in the elimination of mercury, it is evident that this organ, in case it is already diseased (nephritis, amyloid degeneration), may become greatly endangered when mercury is administered.

The unfavorable influence of mercurial treatment in the presence of constitutional diseases and cachexiæ, in so far as these are not caused by syphilis, should also be emphasized. In the case of sufferers from *tuberculosis*, *malaria*, *alcoholism*, *various degenerations*, *anæmia*, *hemorrhagic diathesis*, etc., the condition may be markedly aggravated by the exhibition of mercury. Nicolich indeed has reported the case of a robust man who was addicted to alcohol, in which death followed six inunctions (each of 3 gm.), which had been ordered by an oculist. In the hemorrhagic diathesis especially, a mercurial treatment is dangerous, since it many induce a pernicious anæmia.

Poorly nourished, scrofulous individuals and those who have a tendency to suppuration and necrosis of the bones do not always bear mercury well, and this is also the case when syphilis has assumed a galloping, malignant form. In these cases a tonic treatment or perhaps the use of iodine is indicated, the latter acting more favorably than mercury, even in the early stage of syphilis, in debilitated subjects.

Patients improve with marked rapidity under this treatment, and may even be able to take mercurial preparations later with benefit, if the drug should become necessary.

The following observations show that some individuals with an apparently perfectly healthy constitution may present the gravest even lethal symptoms of intoxications after ordinary doses of mercury, and accidents of this kind, moreover, have been observed after the use of nearly every one of the modes of application of mercury. H. von Zeissl observed the occurrence of a stomatitis one day after the first insufflation of calomel on the conjunctiva. T. P. Sillard records a case from St. Vincent's Hospital in Dublin, in which, after the use for three days of a pill consisting of rhubarb and mercury, a man presented symptoms of grave hydrargyrosis (ulcerous stomatitis), which terminated in death.

Grave mercurial poisoning has frequently been observed after inunction of unguentum cinereum for pediculosis, and in some of the recorded cases the individuals died in a few days (John Lowe Buchner). Inunctions also, as used in every-day practice in the usual doses in the treatment of syphilis, have repeatedly induced grave symptoms of intoxication. Thus Virchow, in a report to the Berliner medicinische Gesellschaft, mentioned having observed the occurrence several times of pseudomembranous enteritis and grave affections of the kidneys after the external use not only of corrosive sublimate, but also of blue ointment. He mentions one case especially of a laborer, thirty-one years of age, suffering from constitutional syphilis (arachnitis basilaris), who at autopsy was found to have a beginning pseudomembranous enteritis after fifty inunctions of blue ointment within fourteen days, each consisting of 5 gm. The discussion following this report is of interest. In this Jacusiel mentioned the case of a patient to whom he had himself administered 2 gm. of unguentum cinereum by inunctions, and who had until then always passed a formed stool, but was taken twenty-four hours later by characteristic dysenteric bloody mucous stools, accompanied by fever and violent abdominal pains. Poelchen observed the occurrence of pseudomembranous enteritis after a daily inunction of 3 gm. of blue ointment; in six cases he found post mortem the lesions of mercurial dysentery following inunctions.

In two cases Neisser observed after five and seven inunctions respectively a most alarming stomatitis, which lasted for weeks; in one case a large slough was thrown off from the back of the tongue, leaving an annoying scar. In one case I was able to demonstrate in a robust man a necrosis of the upper jaw, which had appeared after a regularly conducted course of mercurial inunctions.

Those cases are still more mysterious in which there is a reaction to inunctions with very grave symptoms, although the patients had borne the same treatment very well several years previously. Fournier in his work mentions an experience of this kind. A robust man, of athletic build, had been treated by Fournier for cerebral syphilis and cured. A few years later a course of inunctions was administered to this patient on account of a grave relapse of cerebral syphilis. These inunctions had been employed the first time with great benefit and without any inconvenience whatever, in increasing doses of 6, 8, and 10 gm. In spite of all care and attention, a grave hydrargyrosis accompanied by stomatitis was "suddenly" developed (how much of the blue ointment had been employed up to this time is not stated), which nearly brought the patient to the grave. Fournier concludes his description with the following words: "La langue grosse comme un saucisson, vint faire hernie hors de la bouche et pendre au devant du menton; toute sa face supérieure se sphacéla; pendant une dizaine de jours, j'eu détachai matin et soir des lambeaux mortifiés, jaunâtres ou noirâtres; c'etait un spectacle nauséeux et hideux. Et cette stomatite demanda plus de six semaines pour guérir!"

Similar observations made such an impression on Fournier that he does not hesitate to confess that he was one of those who had had cause to fear the employment of mercury by inunction.

Many deaths have been attributed improperly to the inunctions as such, but this is not always just, and certainly the deaths reported by Lewin from Koch's Institute and from his own clinic cannot be laid directly to the inunctions. In spite of the superficiality with which Lewin reports Koch's case, we may nevertheless assume with confidence that it was one of a grave hemorrhagic diathesis or at least of grave secondary anæmia. A builder, twenty-four years old, suffered several attacks of epistaxis, and his sight was failing. After a number of inunctions he was suddenly attacked with spitting and vomiting of blood, accompanied by a bloody dysentery, from which death resulted. The record of the autopsy mentions colitis, nephritis, fatty degeneration of the heart, and anæmic atrophy of the optic nerve as being present. In Lewin's own case a hemorrhagic diathesis was also present. That patients of this class are greatly endangered

by the exhibition of mercury we have already stated, but if we except those accidents which have occurred in cases of hæmophilia, nephritis, phthisis, and the like, as well as those following the exhibition of exceedingly large doses of mercury, not one single case ending in death —and this should be especially emphasized—can be referred to the action of the drug alone. For not a single report regarding this will bear a critical investigation, as Ullmann, Jullien, Balzer, myself, and others have demonstrated. I may, however, briefly review two cases on account of the authority of those over whose names they have been reported. One of these is the case of Hallopeau, with which, however, Hallopeau had nothing to do in fact; if indeed he had made the injections himself, he would no doubt have exactly adhered to the dose which knowledge and experience have laid down, but the patient was not treated by himself at all, and Hallopeau only reports that some physician had administered the simply frightful amount of 3.5–4.0 c.c. of the thirty-per-cent. solution of gray oil, in five injections, at intervals of eight days. Under such circumstances no one can be surprised that this case had a lethal ending. This report was critically analyzed by Paul Raugé in the *Bulletin Médical* for 1888. The second case was one reported by Kaposi. At the First International Congress of Dermatology and Syphilography (*Comptes rendus*, Paris, 1890), Kaposi, in speaking of this case, said that "ten days after the first injection an ulcerating gingivitis developed and there supervened a diarrhœa which could not be arrested." Also in a clinical lecture published in the *Wiener medicinische Presse* for 1890 he said that "the patient presented the most intense symptoms referable to the intestine and kidney after one single injection, and died six weeks after this injection. If this is the fact, that the patient presented the most dangerous symptoms after the first injection, then it was certainly unjustifiable to administer to the same patient, as we learn from a lecture delivered by Kaposi at Prague ("Verhandlung des ersten Congresses der deutschen dermatologischen Gesellschaft," 1889) that he did, nine or ten more injections. We may well ask what was expected to follow this procedure?

Louis Jullien remarks in this connection that not a single case of poisoning of this kind can withstand a critical analysis, for the untoward results were always due either to error or to grave imprudence.

In reviewing these and other cases which have been reported, we are forced, after a careful examination of the facts in each case, to the conclusion that inunction is the form of treatment which leads in otherwise healthy individuals most frequently to grave complications and to fatal intestinal disturbances. The amount of mercury incorporated into the body in inunctions is, as it were, uncontrollable.

Still another objection to these inunctions is that the effects of the mercurial vapor, always developing with inunctions, which should not be lightly thought of, are with difficulty kept from the attendants.

Prophylaxis of Hydrargyrosis.—The eminently curative power over syphilis which mercury possesses makes its use obligatory, yet, as we have seen, the use of the drug may be dangerous. I have deemed it proper carefully to describe the dangers of mercury, but we shall now consider how these dangers may be diminished and reduced to a minimum.

In the first place, the patient should not only be carefully examined as regards his lues, but also as to his organism, *i.e.*, as to every one of his organs; we should also not neglect to take careful notes of the previous history of the case. While the objective examination will inform us of the presence of other diseases, the previous history frequently reveals certain seemingly unimportant facts which may lead to the discovery of grave constitutional anomalies. The casual remark of the patient that he bleeds long and much, or develops black and blue spots after slight injuries, will make us hesitate, and lead us to suspect a hemorrhagic diathesis. Data concerning diseases of the past and the disposition to disease of certain organs which they have induced, hereditary disposition to certain diseases, are readily obtained in this way, and are important hints to the physician.

If the syphilitic patient is suffering from any other grave disease, such as nephritis, tuberculosis, malaria, alcoholism, amyloid degeneration, anæmia, hemorrhagic diathesis, etc., if he is an invalid independent of his syphilis, a mercurial course should not be attempted, or the system should be previously strengthened by proper treatment. If the nutrition is fair, and even if the patient is suffering from albuminuria, a carefully conducted mercurial course may very properly be attempted; the existence of the complication must, however, never be lost sight of. If the intestinal tract is disturbed, this must be regulated before mercurial treatment is commenced; it should also be an imperative duty to heal lesions and injuries found within the oral cavity, to treat carious teeth, and to remove any stumps which irritate the mucous membrane previous to the institution of a mercurial course.

Should the symptoms of nephritis be discovered in a syphilitic patient, we should consider whether the affection of the kidney may not be directly or indirectly related to the constitutional syphilis; the reader is referred to what has been previously said on this subject in regard to this.

Patients suffering with malignant syphilis, as a rule, do not bear

mercury well, since in these cases syphilitic infiltrations rapidly break down, ulcerating processes enlarge, and the system becomes debilitated by fever. These patients must therefore be first placed under the most favorable hygienic conditions and upon a proper diet, and iodine or sarsaparilla should be early administered, together possibly with iron or arsenic. In this manner the constitution is strengthened, and if a cure has not been effected in the mean time a careful treatment with mercury may now be of benefit. It would certainly be a great gain if we were to possess some mercurial preparation or to discover some mode of application by which the disease could be effectually controlled while the dangers of hydrargyrosis were obviated. Although we have constantly endeavored to gain this end, we have not as yet succeeded. It is rather true that the more effective a method of treatment the earlier must we expect symptoms of intoxication, although fortunately we are not compelled to admit the converse that the value of the method of application is to be measured by the severity of the hydrargyrosis. Our endeavor should therefore be to employ those precautionary measures which on the one hand are demanded by the individuality of the patient and on the other by the mercury in general and its various modes of application in particular.

We will now discuss how the patient is to keep himself during a mercurial course, and what the physician should do in case symptoms of intoxication make their appearance. We should realize that we have no measure at command to prevent mercurialization with certainty; on the other hand we are able to hold in check or to diminish disagreeable and aggravating complications. This is easiest attained if the plain laws of hygiene are also strictly carried out during the mercurial treatment. I have repeatedly observed that the treatment is the better borne the more a rational mode of life and scrupulous cleanliness are adhered to. The patient should guard against overloading the stomach, excesses in venere et baccho, keep away from entertainments which extend far into the night, avoid all excesses and harmful influences, as for example badly ventilated and smoky rooms, etc. He should rather endeavor to live on plain food, not to exceed his normal hours of labor, to ventilate his dwelling-place thoroughly, and to get much or at least sufficient sleep.

In the same manner, the usual care of the skin and of the mucous membranes should be well attended to. For, as a matter of fact, individuals who are addicted to great cleanliness and have good teeth suffer less from stomatitis than those who neglect the toilet of the mouth and suffer with poor and carious teeth. A possible mercurial stomatitis is therefore rendered much more tolerable if we in-

sist from the beginning on a scrupulous care of the teeth and the oral cavity, for which purpose tooth brushes (with or without tooth powder or tooth soap), gargles (see Nos. 3–14) should be frequently used, especially after meals. It is well besides (as previously mentioned) to have carious teeth, especially stumps of teeth, which irritate the mucous membrane removed, and absolutely to interdict the use of tobacco in whatever form. Uneducated patients should be trained for a few days in all these things when therapeutic intervention is not immediately indicated, or they should receive only small doses of mercury during the early period of treatment.

Any causes which are liable to induce intestinal disturbances should also be as much as possible avoided. It is not improbable that irritation of the intestinal tract by an irrational diet, etc., during mercurial treatment may cause the appearance of disturbances much earlier than would otherwise be the case. It is no less desirable that the patient avoid the use of strongly seasoned food, too much strong coffee, tea, alcohol, and other substances which have an irritative action on the kidneys.

Bodily overexertion (wheeling, gymnastic exercises, etc.) should be avoided as carefully as mental overwork.

During the whole period of treatment and also later, the patient should be under careful observation; he should besides be cautioned to notify his physician at once should any disturbance occur. Under all circumstances, a frequent examination—if possible, at least twice a week—should be made, and in this special attention should be paid to the conditions previously described, particularly, however, to the three cardinal symptoms—stomatitis, albuminuria, enteritis.

Treatment of Hydrargyrosis.—Should even a slight sign of mercurialization be discovered during treatment, the local as well as constitutional mercurial treatment must at once be abandoned. It would, however, be, to say the least, naïve to assume that with the cessation of treatment the continued action of the mercury already taken also ceases; it is impossible that the mercury which has been rubbed into thousands and thousands of pores, and is still contained in the tissues, should at once cease to be active. At first thought we might be led to believe that the action of the mercury internally administered would cease at once on its discontinuance; but this would also be incorrect. It has already been said that mercury can be detected in the urine for a long time after the last dose of calomel has been administered. In the case of subcutaneous injections of insoluble salts of mercury it would be possible to remove the deposit, and to arrest any further action of the mercury only by excision. The last recommendation is, in fact, worthy of a more minute consideration.

Should the stomatitis or nephritis or colitis take on an especially grave character, the mechanical removal of the mercurial foci present might, at all events, be attempted. If the injection has been made deeply into the tissues, as I recommend, we shall probably not meet with any difficulty in locating the later doses of mercury by palpation, cutting down on them, and removing a greater or lesser portion by means of sterilized pieces of cotton, washing out the rest of the deposit by a strong stream of carbolized water; we may even cut out with the knife and scissors portions of the tissue in which the medicine is embedded. This cannot be done if the injections have been made into the muscular tissues of the nates; for it would not be an easy matter to reach with the knife all of a number of recent injections in this part; and moreover, the search for them would necessitate a number of deep incisions.

Fortunately, mercurialism will never lead to dangerous symptoms, if the necessary caution has been observed in the treatment, and if the boundaries previously marked out have not been passed, so that a simple regimen is usually sufficient. With this the preventive rules, described above, are to be observed with redoubled care. The oral cavity, if stomatitis is present, should be rinsed very frequently, if necessary every half or quarter of an hour, and any mercurial ulcerations which may be present should be touched with a strong solution of the chlorate or of the permanganate of potassium, cauterized with nitrate of silver, hydrobromic acid (17), or some other caustic. The diet should be restricted mainly to milk, eggs, and chopped meat. When intestinal disturbances are present, rest is to be recommended, and if necessary, opiates may be administered. The ventilation of the living-apartments is also of the greatest importance.

The symptoms of mercurialism will generally disappear very rapidly if the treatment has been carefully conducted. As salivation and stomatitis improve, the albumin will also disappear from the urine, and any intestinal disturbances which may be present will gradually subside.

A cure will result in a few days, or at the end of one or two weeks, according to the severity of the hydrargyrosis; in rare cases later still. If the indications should now still be present, there will be no reason why mercury should not be again administered. It has indeed been remarked that patients often bear the mercury better now than formerly, though occasionally the tolerance to a second mercurial course seems to be lessened. The rules above detailed should therefore be carried out with even greater punctiliousness.

Occasionally hydrargyrosis manifests itself only some time after treatment has been concluded; these belated symptoms of mercurial-

ism may occur after inunctions as well as after injections and internal treatment. The treatment of this condition is the same as that just described.

Pulmonary Embolism.

I shall devote just one word to the unwelcome occurrence of embolism in the lungs. This may be avoided, or at least reduced to a minimum, if (1) the insoluble mercurial preparations are employed only in the manner recommended by me; in this way the amount of fat to be injected is reduced at least to a tenth; and (2) if the injections are not made into the muscular tissue of the nates, but deeply under the skin in the back, for the reason that in the latter situation the danger of emptying the contents of the syringe into a large vein, which has repeatedly happened in the nates, is not nearly so great.

IODINE.

Iodine was used for medicinal purposes, including the treatment of syphilis, not long after its discovery in 1811 or 1812; but we are indebted to William Wallace for a better knowledge of one of the most valuable antiluetic remedies, namely, *iodide of potassium*. Since that time the preparations of iodine have been frequently and with great advantage prescribed in syphilitic affections, the products of which they frequently dissipate much more rapidly than does mercury. The first place, and rightly so, is even to-day held by *iodide of potassium*, which is administered in daily doses of 0.25 to 1.0 (gr. iv.–xv.), 2.0 to 4.0 (ʒ ss.–i.), and if necessary even larger quantities. In certain obstinate cases it may be necessary to administer still larger doses. By gradually increasing the dose I have reached as much as 10 and even 20 gm. (ʒ iiss.–v.) a day, and have succeeded thereby in curing syphilides finally which had resisted other treatment for a long time. I have, moreover, been able to convince myself, during my therapeutic experiments with psoriasis, that still larger doses of iodide of potassium—I have used as high as 40 gm. (ʒ x.) a day—are well borne; in one patient only, the secretion of urine diminished and was altogether arrested for twenty-four hours, but after the medicine was discontinued the anuria disappeared.

Solutions are to be preferred under all circumstances, and are to be taken—like all preparations of iodine—twice or three times daily immediately after meals; no preparation of iodine should be taken on an empty stomach. Should pain in the stomach or diarrhœa nevertheless occur, opium should be added; if constipation is produced, syrupus mannatus may be employed (105).

If iodide of potassium is to be administered in the form of pills, milk-sugar and lanolin, according to my recommendation, should be used as an excipient (111).

Some individuals may bear *iodide of sodium* better; this may be prescribed in the same manner. *Iodide of rubidium* has also given me excellent results. *Iodol* has frequently been found very effective, and sometimes in cases in which iodide of potasium had failed me; it is to be given in doses of 0.5 gm. (gr. viii.) from two to six times a day (114).

Milder remedies are found in *tincture of iodine*, which should be given diluted in water (110) or in *iodoform* which is prescribed in pill form (115).

In some cases, as will be explained later on, the simultaneous employment of *iron* preparations is indicated; we should here make use of Blancard's pills (116), or some similar preparation (117). Syrup of the iodide of iron fulfils the same purpose, excepting that it easily decomposes, but this decomposition may be avoided by keeping a clean piece of iron wire in the syrup. It may be prescribed with simple syrup or some other syrup (118).

If the stomach is to be considered, or if for any other reason preparations of iodine cannot be administered internally, rectal administration, which has been especially warmly recommended by Köbner, will prove practical. The most simple form is in that of clysmata containing each from 1 to 4 gm. (gr. xv.–lx.) of iodide of potassium, dissolved in water or milk (112). In one of my patients, who was suffering with a gumma of the medulla oblongata, deglutition was impossible; on account of a paralysis of the sphincter the administration of iodide of potassium per rectum was also impracticable, and I found myself compelled to inject the remedy subcutaneously. By employing a fifty-per-cent. solution we can administer doses of 0.25 to 0.5 gm. (gr. iv.–viii.) of the iodine salt very easily, and it is really surprising how promptly involution of syphilitic products may be obtained in this way. One objection to the subcutaneous injection of iodide of potassium is that it is very painful; by the addition of codeine, however, the pain may be somewhat diminished (113).

Mineral waters which contain iodine and bromine are used not only as a drink, but also for bathing. Among the spas of Southeastern Europe visited for this purpose we may mention Hall in upper Austria, Csiz in Hungary, Darkau in Silesia, Lippik in Slavonia, Luhatschowitz in Moravia, and Iwonicz in Galicia. The efficacy of these waters is markedly enhanced when iodide of potassium or mercury is employed at the same time.

Iodine is absorbed with extraordinary rapidity, and may be de-

tected in the saliva after from one and one-half to ten minutes, and later in the urine, bile, milk, and other secretions. By far the largest proportion is excreted by the kidneys, and that very rapidly within twenty-four hours; a small portion, however, seems to be retained in the circulation for some time, but is finally, perhaps after the lapse of weeks, eliminated by the kidneys. In nursing women iodine can be found in the milk for several days after its administration has ceased, even when none can be detected in the urine. Welander found it present in the urine of new-born children (who had not yet begun to nurse) of women who were taking iodide of potassium.

Iodism.

Certain symptoms are occasionally met with during the administration of iodine which may be more or less detrimental to the system, occasionally even threatening death. We are naturally not dealing here with acute iodine poisoning produced by the ingestion of large quantities of iodine (say tincture of iodine), and which runs its course under the picture of a severe gastroenteritis. We shall only very briefly touch on iodism, as it presents itself in more or less severe or mild form during the internal administration of iodine.

Some individuals are seized after each dose with intense headache. As a rule, one of the early symptoms is a feeling of dryness in the nose, followed by a coryza. The excessive secretion and irritation are not confined, however, to the mucous membrane of the nose only, but extend also as a rule to the neighboring cavities and tubes. Occasionally salivation occurs, accompanied by stomatitis and swelling of the salivary glands; and sometimes we note a sore throat, lacrymation (conjunctivitis), and pain in the frontal sinuses. The face and eyelids may also become reddened. The catarrhal affection, as I have had occasion to observe several times, may also attack the mucous membrane of the rest of the respiratory tract, of the glottis, the trachea, and the bronchi; dangerous œdema of the glottis has also been seen by me and others. As a rule the patients complain of an irritation which leads to coughing and of pain in the chest; fatal pneumonia and pleurisy have even been observed. An acne makes its appearance on the integument, especially of the face, forehead, and back; or blebs are formed, occasionally on a spot of cutaneous infiltration, or the skin becomes affected in the form of a roseola or purpura. In one case I observed the appearance, after the administration of large doses of iodine, of spongy vegetations from the size of a pea to that of a chestnut on the skin of the nose, the hairy scalp, and the back. The presence of iodine has been demonstrated in the glands and in the secretion of iodine eruptions.

An atrophy of glandular organs (mammæ, testicles) may occur after the long-continued use of iodine preparations. A colleague of mine, who made frequent applications of tincture of iodine to his enlarged thyroid gland, observed that there was a diminution in size of his testicles a short time after each application. Secretion and excretion are not always affected in the same way. The saliva is at times increased, at times diminished; the secretion of milk is markedly lessened; the urine becomes scanty and contains albumin; the menstrual flow seems to be more copious.

Of all the symptoms of iodism acne is the least dangerous; so long as this is alone present, we need not feel constrained to stop the administration of iodine. If headache regularly occurs with the ingestion of iodine, it may be readily relieved by antipyrin (120, 121). As soon, however, as symptoms on the part of the mucous membrane of the respiratory apparatus make their appearance, the further use of the remedy should be at once stopped. Certain individuals show such a marked idiosyncrasy in relation to the remedy that comparatively small doses may produce severe iodism. The symptoms of intoxication will, as a rule, disappear when the iodine is discontinued, and the remedy then generally agrees with the patient better than before. When there is a tendency to iodism, belladonna may be added to the iodine solution (109). We should also remember that irritating combinations may be formed when an iodine and mercury therapy is pursued together. When the patient is taking iodide of potassium internally, we should be careful not to insufflate calomel on the conjunctiva, for the reason that the iodide of potassium, which can be detected in the tears within a few minutes, will convert the calomel into mercurous and mercuric iodide, which act badly in the presence of common salt or iodide of potassium, and exert a caustic effect on the conjunctiva (Bellini, W. Schläfke). We should also keep in view the possibility that whenever mercury and iodine are administered together, this dangerous combination of the two salts may take place.

The best results are obtained by the iodine treatment in the later stages of syphilis, especially when gummatous products are present. Cutaneous serpiginous syphilides, gummata of the subcutaneous tissue, the fasciæ, and the muscles, sarcocele syphilitica, syphilis of the bones and joints, ulcers of the tongue, palate, and pharynx, affections of the larynx, gummata of internal organs, the nervous centres, and the organs of special sense, as well as many relapses occurring at a late stage, are cured by preparations of iodine in a manner which is simply surprising.

Although the early forms of syphilis, especially its first eruptions, react only very little to iodine as a general rule, we nevertheless

occasionally find that early relapses are markedly improved by it. The remedy proves very effective also in the relief of neuralgic attacks and pains in the bones and joints, which precede or accompany the early eruption; these are as a rule speedily removed by a few doses of iodide of potassium or of iodine and antipyrin (120). Iodine seems also indicated in those cases of early syphilis which are not suitable for a mercurial treatment. In the case of tuberculous, scrofulous, and cachectic individuals, those who are debilitated by want and suffering, and those in whom the disease has taken on an acute, malignant form, the primary indication is for the institution of an improved hygiene and tonic treatment, but treatment by iodine as a specific is also much more salutary in such cases (119). Occasionally these patients may be subjected later, when the general health has improved, to a careful mercurial course.

In very grave, desperate syphilitic affections, or when the disease products are localized in functionally important or vital organs, we have recourse simultaneously to a very energetic mercurial treatment and an iodine treatment, administering the mercury as a rule in the form of injections, inunctions, or smearings, while the iodine is taken internally. We are thus frequently able to prevent injuries with which vital parts are threatened.

When the symptoms are not urgent, we may generally begin with small doses; even these frequently induce a marked involution of the specific lesions; should we, however, observe no improvement, or if the improvement suddenly ceases, we may increase the doses. It is only in cases which demand rapid, energetic interference, as in syphilis of the nervous system, of the organs of special sense, etc., that we are justified, even compelled, to enter at once upon a radical treatment. The form of the disease and the condition of the patient should influence us in our therapeutic endeavors. In cases in which a syphilitic child has been born, the parents should be subjected to an antisyphilitic treatment, even when they present no marked signs of the disease. In a case of this kind, we can, of course, depend only on a purely subjective estimation, but may at the most gain a few more specific indications for treatment from the gravity of the hereditary lues; too much treatment in such a case is always better than too little. The treatment should therefore extend over several weeks, during which time mercury and iodine preparations may be used quite extensively. I also make a practice usually of injecting deep under the skin of the scrotum, in the neighborhood of each testicle, 0.01 to 0.02 c.c. of gray oil. Treatment, for the rest, should be continued so long as improvement is noted within the boundaries of a rational dosage. It is judicious, however, to continue treat-

ment for two or three weeks after the total disappearance of all symptoms.

When the treatment is prolonged, it will be judicious to discontinue the remedy after a few weeks, for a longer or shorter period, even though the symptoms have not yet all disappeared. After such an interval a return to the medication will, as a rule, yield much better results; or else we may as time goes on employ mercurial and iodine preparations alternately.

Non-Specific Remedies.

Unfortunately we do not always gain the desired result when using the so-called specifics; though there may be an improvement at first, this may in rare cases cease and the local lesions may appear to grow worse after a time, while the general condition of the patient is obviously worse; in this respect the forms of syphilis known under the names of malignant and galloping (see above) are to be dreaded especially. Here we shall not usually derive any benefit from the mercurial or iodine preparations, and shall do well to discontinue them. An inspissated sarsaparilla decoction, especially a tonic treatment, will be most efficacious here; fresh air, good food with a glass of wine or brandy, and proper local treatment will yield the best results; the conscientious physician will also have to decide, during the course of treatment, whether it is necessary to prescribe other tonic preparations, such as iron, the simple bitters, and arsenic (116–118, and 123–127).

In cases in which the long-continued use of mercury and iodine has produced a cachectic condition in the patient, we can derive no benefit from the continuation of the medicine, though syphilis be still present. In such cases I have found the administration of sarsaparilla combined with good nursing and the strictest observance of all hygienic rules to be of great services, exerting the most beneficial influence on the patient's nutrition. This remedy, which was employed in the treatment of syphilis at the beginning of the sixteenth century, is used even to-day. Two decoctions, decoctum Zittmanni and decoctum Pollini, which mainly consist of sarsaparilla, have maintained their reputation for a long period, and we cannot deny that a favorable influence on old forms of syphilis is exerted by Zittmann's decoction. I am in the habit of prescribing 200–300 gm. (℥ vii.–x.) of the strong as well as of the weaker preparation, to be taken during the day. Should the decoction move the bowels too powerfully, the senna leaves may be left out.

I have long since ceased to order my patients to drink large quan-

tities of the sarsaparilla decoction, as the intestinal tract will in time rebel. The *decoctum sarsaprillæ inspissatum* (122) is on the other hand very well borne; even when it is taken for a very long time I have never seen the slightest disturbances caused by it, and it may therefore be administered to the patient for weeks and months. In several cases, which on account of grave syphilis had been subjected to energetic treatment with mercury and iodine without benefit, I was able to convince myself of the excellent effects of this decoction upon the specific disease, and in others to demonstrate that the general condition of debilitated individuals visibly improved, and that it even became all that could be desired, although a perfect removal of the syphilitic products could not be obtained by the remedy. Nevertheless, I believe that this success was also in a great measure due to the regulated mode of living which I enjoin, whether in private or in hospital practice.

Cachectic conditions and *amyloid degenerations* caused by syphilis are to be treated according to the general rules of medication. Nutritious food, life in the open air, moderate bodily exercise, are the main conditions to be fulfilled; preparations of iron and iodine occasionally have a markedly favorable influence, but outside of this a symptomatic treatment only is indicated. Mineral waters and hot baths are to be employed with caution. Finally in affections of individual organs we should employ the methods that are useful in non-specific diseases of the same parts. Thus in syphilitic diseases of the eye we should be guided in our treatment by general principles; grave affections of the joints caused by syphilis are to be treated in the same manner as arthropathies from other causes; affections of the muscles or nerves occasionally require an after-treatment with electricity. Strictures resulting from contracting cicatrices, which have remained behind in the larynx, pharynx, œsophagus, or rectum, after syphilitic ulcerations will have to be dilated with bougies or cut with the knife, and sometimes we shall be compelled to resort to tracheotomy, gastrotomy, or colotomy, as the case may be. In individual cases an operative removal of the disease focus will be found necessary, when the usual treatment does not lead to a cure and the patient is continuously endangered by the presence of the lesion. In short, the principles of general medicine should always be borne in mind in the treatment of syphilis. These same considerations must also guide us in the choice of climatic or balneological treatment.

Now that we have discussed the usual methods of treatment, it is only left for us to take up a few general considerations.

It cannot be expected of us to enumerate all the views extant on the treatment of syphilis and their changes; we can only in this

work treat of those therapeutic measures which, according to the present views on this disease, are in general use among clinicians.

Those syphilologists who see in the initial lesion the first manifestation of constitutional lues resort at once to constitutional treatment. Those, however, who look upon the initial lesion only as the locality where the deposited virus remains for a time, to become diffused later on, advocate the removal or destruction of this initial product, or they make an attempt to render the virus innocuous, by means of abortive treatment (see above).

Should extirpation or abortive treatment be impossible on account of the unfavorable seat of the lesion, or for other reasons, we may, without prejudice to the view that the initial lesion is purely local, proceed at once to preventive medication with mercury, since we can in this way so influence the system and the virus that the further course of the disease is made milder, or in individual cases altogether arrested. It is recommended, with certain exceptions (see above) not to begin the constitutional treatment until a positive diagnosis of constitutional syphilis has been made.

Together with this, we always lay the greatest stress on proper hygienic conduct, on local treatment, and on the other measures rendered necessary by the locality of the lesion—the application, therefore, of all auxiliary measures afforded us by medical art and science. In some cases syphilitic foci existing for years can be removed solely by a surgical operation.

A careful observance of these rules will afford extraordinarily satisfactory results; gummatous deposits, grave affections of the osseous system, destructive processes of the face, the nasopharyngeal cavity, etc., will be regarded actually as curiosities in patients who have been treated according to these repeatedly emphasized principles; a milder course of the process and finally a cure will be the rule, if we may be permitted to look upon continued well-being, healthy issue, and the possibility of reinfection as signs of the latter. In spite of this favorable experience, however, I must candidly admit that it is impossible in every case to be absolutely sure that relapses will not occur.

Intermittent Treatment.

Alfred Fournier conceived the idea of extending the treatment to five or six years, as a preventive measure against any possible relapses, and so introduced his method of intermittent treatment continued over a long period. This method is based on the idea that syphilis, in accordance with its chronic course, should also be treated chronically. It has long been known and recognized that syphilis quite

frequently leads to the development of characteristic pathological products at intervals of weeks, months, and even years, and it has also been observed that these products usually disappear promptly after the administration of mercury and iodine. Corresponding to these successive eruptions of the disease a method of treatment has been and is even yet followed in suitable cases, which is a successive and chronically intermittent one. While we, however, fit our therapeutic measures to the course of each individual case, Fournier thinks it better to anticipate in every case these successive attacks by the administration of mercury and iodine. His aim is ever to cure the present attack and prevent new outbursts of the disease. In proportion, however, as he found the goal which he desired recede further and further, he also extended his treatment to longer and longer periods, until he reached a course extending over many years.

It is to a high degree instructive in this regard to touch upon the phases which Fournier passed through successively until he reached the last potential of his "successive" therapeutic method. During the fifties and sixties he demanded a specific treatment lasting from nine to twelve months; in the seventies, this period was increased to two years; in the eighties, again, he became dissatisfied with a specific treatment lasting two years and lengthened it to four years; at present, on account probably of the want of success hitherto noted, he declares with ardor that the specific treatment of lues when scientifically conducted should be carried on for five or six years, and even as "cures préventives à longues échéances" that it should be repeated from time to time decades after infection has taken place. Fournier describes the special course of mercurial and iodine treatment lasting six years in an "ideal case" as follows: The patient takes mercury for about two months (for example 10 cgm. of the protiodide daily), when a pause of from four to six weeks is made. The same treatment is then repeated for six weeks, and a pause of from two to three months is again made. Then follows the same succession of medication, suspension, medication, etc. As a general rule, four courses of mercurial treatment would be carried out in the first year, three in the second, and two in the third. He then passes on to the iodine treatment, which extends over from four to six weeks, the medium dose being 3 gm. a day according to tolerance. From four to six treatments of this kind are given in one year, and when necessary they alternate with mercury; the following year three more are given, and the year after that two.

The patient is thus required, according to Fournier's advice, to take mercury for three years, with certain intervals, and for two or three years following, iodine (occasionally in conjunction with mer-

cury). This method of treating syphilis altogether ignores the natural history of the disease.

The course of syphilis, as we have already said, is quite variable, and we should particularly never lose sight of the fact that the disease in any of its stages may end in a perfect cure. Although we are compelled to admit the fact that in not a few patients (especially in those who lead an irregular life and are otherwise careless) syphilis shows its presence by repeated outbursts, or even reappears after an interval of many years, frequently without any apparent cause, it should not be overlooked on the other hand that quite a number of well-authenticated cases have been reported by reliable observers, among whom we may also include Fournier, in which syphilis after a single eruption ended in a definite cure. More than that, impartial observation teaches us that the disease, in an overwhelming majority of cases, becomes extinct with the passing of the irritative symptoms, or as Pick expresses it, that the end of the irritative period in most cases signifies the end of the disease. As we are, however, unable in the beginning to determine in which individuals, *ceteris paribus*, we are to expect that the disease will run a long course, we shall be acting more rationally if we do not permit the treatment to be conducted in a routine manner, but rather regulate it in each case by the course of the disease. If we take a case in which syphilis at the end of several months has run its full course, we shall have good results from any treatment, even from Fournier's, which is to be continued for a series of years, provided that the mercury and iodine are given in proper amounts.

The case will be altogether different, however, if the disease is not so rapidly eliminated, either through the patient's own neglect or through other causes. In these cases, treatment based upon a constant and long-continued observation of the disease as well as of the patient alone can insure any beneficial results.

Fournier's endeavor was certainly animated by the purest humanity when he attempted to anticipate the outburst of the disease and to cure it by an early and prolonged specific treatment. That he was not always able to do this, however, he has confessed himself in several parts of his book, where he admits having not infrequently observed relapses, in the form of syphilis palmaris, after five, six, and eight years, notwithstanding that the patients had undergone the most correct treatment for syphilis according to Fournier's plan. When he recommends the renewed exhibition of mercury in these cases, he adds to his chronic treatment the temporary method recommended by ourselves.

To prove the value of the chronic intermittent treatment Fournier

has gathered a great many statistics, which he arranges in tables. Unfortunately, in spite of all the diligence used in their collection, all these statistics bearing upon the treatment of syphilis are useless. I will mention one of the statistical tables, which has been quoted by others as a proof of the great value of the "successive chronic intermittent treatment," only to show that the opposite of what it was intended to prove may with ease be deduced from it.

Fournier asserts that cerebral syphilis is much less frequently developed when the therapeutic measures recommended by him are carried out, and fortifies his assertion by the following statistics:

Out of 100 cases of cerebral syphilis in which the therapeutic antecedents were perfectly well known, 5 cases were subjected to a severe and prolonged mercurial treatment; in 6 a treatment of medium but insufficient duration was administered; 10 patients were treated for from seven to eighteen months only; 70 underwent a very much shorter treatment (one to six months); in 4 no treatment at all was had, and 5 were treated only with iodide of potassium. Let us now examine the above statistics critically. Fournier says, "in round figures then 5 patients out of 100 had undergone a serious treatment, while 95 had been subjected to a course which was insufficient, short, very short, or insignificant, or to no treatment whatever. From this it follows mathematically that cerebral syphilis is nineteen times more rare after a serious treatment than in patients who have had an insufficient treatment or none at all. According to these statistics, therefore, mercury exercises an efficacious and powerful action in preventing the invasion of the brain by the syphilitic process, and we are consequently justified in regarding it as a preventive of cerebral syphilis."

I must confess it seems to me that the conclusion Fournier deduces from these figures is incorrect. By the same logic he would have to admit that 5 of the 100 patients did not undergo any other but an iodine treatment, while 95 were subjected to other treatment or to no treatment at all, and we could therefore assert with mathematical accuracy that cerebral syphilis occurred nineteen times less frequently after an iodine treatment alone than after a mercurial or no treatment at all. But even more than that, 4 out of the 100 patients suffering from cerebral syphilis had not received the slightest treatment; according to his argument, Fournier would have to conclude that, as 4 patients out of 100 have received no treatment whatever, as against 96 who were in part treated with mercury, in part with iodine, we might reason with mathematical accuracy that cerebral syphilis is observed twenty-four times less frequently in patients who have re-

ceived no treatment at all than in those who have undergone a course of mercurial or iodine treatment.

We are furthermore compelled to emphasize the fact that a forced mercurialization exerts an unfavorable influence on the syphilitic process. I have been able to convince myself of this fact in my own patients, and still more so in those of other physicians, and have repeatedly demonstrated that a cure could be obtained in these cases only after the mercury was discontinued. We must not overlook the additional fact that patients treated by the chronic method quite frequently lose ground and suffer from digestive disturbances and insomnia; they are most frequently, however, attacked by manifold disturbances of the nervous system. The treatment extending over years, therefore, quite frequently exerts an aggravating influence on the development of the disease, and also affects the constitution of the patient in a depressing manner.

Finally, the patients treated by this method become habituated to the action of mercury and iodine, so that when relapses occur, as they sometimes do, even under Fournier's treatment, the system does not respond to these remedies, and thus we are deprived of our most effectual weapon.

From what has been said, it is evident that the treatment of syphilis calls for the greatest care. All the circumstances should be carefully studied in each individual case before the form of treatment is chosen. At the same time we should not forget that individual patients, especially those who have received an overdose of mercury and iodine, are most certainly restored to health by keeping from them the specific remedies, especially mercury. We must, however, learn to individualize, and exert the greatest care in each separate case. The greater number of patients who have in the beginning undergone a rational hygienic and therapeutic treatment may expect a perfect cure. Medical supervision is nevertheless strongly to be recommended for a long period, so that the first appearance of any relapse may be at once detected. We should therefore warn every patient in the beginning that his best chances for the cure of syphilis are to be found in following the repeatedly mentioned, absolutely necessary rules; but that, in view of the nature of the disease, he will have to subject himself to observation for a long period. Those patients usually fare the worst who are continually changing their physician, either from impatience at the long duration of the disease or because they are compelled by business reasons to be moving about continually from city to city or from country to country.

Formulæ.

1. Acid. carbol..... 1.0–4.0 (gr. xv.–lx.)
   Aq. fontan. (dest.)..... 200.0 (℥ vi.)
S. For lotions and dressings.

2. Hydrarg. chlor. corros..... 0.1–0.2 (gr. iss.–iij.)
   Aq. font. (dest.)..... 200.0 (℥ vi.)
S. Use as No. 1.

3. Potassii chloratis..... 2.0–4.0 (ʒ ss.–i.)
   Aq. fontan..... 200.0 (℥ vi.)
S. As No. 1. Also for mouth-wash and gargle.

4. Zinci sulphocarbol..... 5.0 (gr. lxxv.)
S. Make five powders, one to be dissolved in a pint of water. Use as No. 3.

5. Sodii boratis..... 10.0–25.0 (ʒ iiss.–vi.)
S. Make five powders and use as No. 4.

6. Zinci sulphocarbol..... 1.0 (gr. xv.)
   Aq. fontan. (dest.)..... 250.0 (℥ viij.)
   Tinct. myrrh..... 1.0 (♏xv.)
S. To be mixed with two to five times its quantity of water, and used as a mouth-wash and gargle.

7. Zinci sulphocarbol..... 1.0–2.0 (gr. xv.–xxx.)
   Aq. fontan. (dest.)..... 250.0 (℥ viij.)
   Aq. menth. pip..... 50.0 (℥ iss.).
S. Use as No. 6.

8. Tinct. iodi (or gallæ or krameriæ)..... 10.0 (ʒ iiss.)
   Aq. fontan..... 500.0 (O i.)
S. Mouth-wash and gargle. Also for use as No. 20.

9. Acid. tannic..... 10.0–20.0 (ʒ iiss.–v.)
S. Make four powders and dissolve one powder in a pint of water. Use as mouth-wash.

10. Acid. tannic..... 2.5–5.0 (gr. xxxviij.–lxxv.)
    Aq. fontan. (dest.)..... 500.0 (O i.)
S. Use as No. 8 or 20.

11. Tinct. opii..... 5.0 (♏lxxv.)
    Aq. fontan..... 500.0 (O i.)
S. Use as No. 8.

12. Potassii permanganat..... 0.05–0.5 (gr. ¾–viiss.)
    Aq. font. (dest.)..... 500.0 (O i.)
S. Mouth-wash and gargle.

13. Chloral hydrat..... 5.0–10.0 (gr. lxxv.–cl.)
    Aq. font. (dest.)..... 500.0 (O i.)
S. Use as No. 3.

14. Balsam. peruvian..... 5.0 (♏ lxxv.)
Alcoholis absol..... 20.0 (℥ v.)
Aq. font..... 500.0 (O i.)
S. Use as No. 8.

15. Tinct. krameriæ,
Tinct. gallæ (or iodi).....āā 20.0 (℥ v.)
Tinct. myrrh..... 10.0 (℥ iiss.)
S. As a paint in gingivitis or stomacace.

16. Carbon. veget. præp..... 50.0 (℥ iss.)
Zinci sulphocarbol..... 1.0–2.0 (gr. xv.–xxx.)
Pulv. rad. ireos flor..... 5.0 (gr. lxxv.)
S. Tooth powder.

17. Acidi hydrobromici..... 20.0 (℥ v.)
S. For painting in ulcerous stomatitis.

18. Acidi lact..... 0.2–1.0 (gr. iij.–xv.)
Æther. sulph..... 15.0 (℥ ss.)
Spts. vini rectific..... 5.0 (♏ lxxv.)
S. For painting in leucoplakia and lingua geographica.

19. Balsam. peruvian.,
Alcoholis absol.....āā 10.0 (℥ iiss.)
Æther. sulph..... 20.0 (℥ v.)
S. Use as No. 18.

20. Hydrarg. bichlor..... 0.05–0.2 (gr. ¾–iij.)
Aq. destill..... 200.0 (℥ vi.)
S. 20 to 40 c.c. (℥ v.–x.) to be inhaled in laryngitis by means of a spray-producer daily or two or three times a week. In the latter case Nos. 10, 21, 22, or 24 should be inhaled on the other days.

21. Zinci sulphocarbol..... 0.5–2.0 (gr. viij.–xxx.)
Aq. fontan..... 200.0 (℥ vi.)
S. Use as Nos. 1 and 10.

22. Arg. nitratis..... 0.01–0.1 (gr. ⅙–iss.)
Aq. destill..... 200.0 (℥ vi.)
S. Use as No. 20.

23. Cupri sulph..... 0.2–2.0 (gr. iij.–xxx.)
Aq. destill..... 200.0 (℥ vi.)
S. Use as No. 1.

24. Zinci sulphocarb.,
Alum.....āā 0.5–2.0 (gr. viij.–xxx.)
Aq. destill..... 200.0 (℥ vi.)
S. Use as Nos. 1, 10, and 20.

25. Zinci sulphocarbol..... 50.0–100.0 (℥ iss.–iij.)
Glycerini..... 50.0 (℥ iss.)
Aq. font. (dest.)..... 200.0 (℥ vi.)
S. For the impregnation of cotton or gauze tampons; to be applied once or twice a week for one-quarter to one-half an hour, when profuse vaginal secretion is present.

26. Alum gauze—five yards of gauze to be impregnated in a large vessel with:

Spts. vini	500.0	(O i.)
Glycerini	250.0	(℥ viij.)
Aluminis	100.0	(℥ iij.)

S. To be used as No. 25.

27. Tannin gauze.

S. To be prepared and used as No. 26.

28. Black oxide of mercury gauze—five yards of gauze to be impregnated (like No. 26) with:

Hydrargyri oxidi nigri	10.0	(℥ iiss.)
Alcoholis	300.0	(℥ ix.)
Glycerini	150.0	(℥ ivss.)

S. To be used as a dressing for syphilitic (gummatous) ulcers, adenitis, etc.

29. Pulv. iodoformi (iodoli or dermatoli) ..... 10.0 (℥ iiss.)
Gummi arab.,
Amyli.....āā 1.0 (gr. xv.)
Glycerini..... 1.0 (♏ xv.)

S. Make bacilla of different sizes. For use in ulcers of the urethra, the anus, etc., and in fistulæ.

30. Iodoform. pulv. (iodoli or dermatoli)..... 8.0 (℥ ij.)
Ol. theobromi,
Gummi arab.....āā 1.0 (gr. xv.)
Aq. destill..... 0.5 (♏ viij.)

S. Make bacilla and use as No. 29. (Softer pencils than the preceding.)

31. Iodoform. pulv. (or iodoli)..... 10.0 (℥ iiss.)*
Ol. theobromi..... 5.0 (gr. lxxv.)

S. Make bacilla and use as No. 29.

32. Ol. cinerei 20 per cent. (No. 80)..... 50.0 (℥ iss.)

S. Inject a few grammes into the urethra, if syphilitic products are present there.

33. Ung. ciner. lanolin. fort. (No. 77)..... 3.0 (gr. xlv.)
Ol. theobromi..... 2.0 (gr. xxx.)
Mass. tragacanth..... 5.0 (gr. lxxv.)

S. Make bacilla and use as No. 29. (Flexible gray pencils.)

34. Ung. hydrarg..... 5.0 (gr. lxxv.)
Ol. theobromi..... 10.0 (gr. cl.)

S. Make 10 globules, to be placed in the vagina in indurations and gummata of the cervix; these globules are also readily borne by pregnant women.

35. Ung. hydrarg ..... 10.0 (℥ iiss.)
Ol. theobromi..... 20.0 (℥ v.)

S. Make 15 suppositories for use in the treatment of papules and ulcerations of the rectum.

36. Hydrarg. ammoniat..... 0.5–4.0 (gr. viiss.–lx.)
Ol. theobromi..... 20.0 (℥ v.)

S. Make 10 suppositories and use as No. 35.

Or,

Iodoform..... 1.0 (gr. xv.)
Ol. theobromi..... 10.0 (ʒ iiss.)
S. Make 10 suppositories and use as No. 35.

37. Ung. hydrarg..... 1.0 (gr. xv.)
Ol. theobromi..... 2.0 (gr. xxx.)
S. Make small suppositories for use in the treatment of chancres within the urethra. The suppository should be placed in cold water for a few minutes to make it firm, and then passed into the urethra, being retained by a strip of emplastrum hydrargyri placed over the meatus.

38. Ung. hydrarg..... 2.0 (gr. xxx.)
Ol. theobromi..... 10.0 (ʒ iiss.)
S. Make bacilla from 5 to 7 mm. thick and from 2 to 8 cm. long. To be used in the treatment of syphilitic ulcers and indurations of the nasal and other cavities.

39. Hydr. chlor. mitis, or Hydrarg. ammoniati... 1.0 (gr. xv.)
Ol. theobromi..... 10.0 (ʒ iiss.)
S. Make bacilla for use as No. 38.

40. Calomel..... 1.0–4.0 (gr. xv.–lx.)
Talc. venet. (or magnes. carbon.) .... 20.0 (ʒ v.)
S. A dusting-powder for use in hyperidrosis pedum, intertrigo, mucous patches of the anus, genitals, etc.

41. Pulv. amyli..... 20.0 (ʒ v.)
Acid. salicyl..... 1.0–2.0 (gr. xv.–xxx.)
(Or zinc. oxid. or dermatoli, 1.0–4.0.)
S. Use as No. 40.

42. Pulv. amyli oryzae..... 30.0 (ʒ i.)
Talc. venet..... 20.0 (ʒ v.)
Pulv. rad. ireos flor..... 2.0 (ʒ ss.)
(Calomel or flor. zinci or acidi salicyl., 1.0–5.0—gr. xv.–lxxv.)
S. Dusting-powder for use as No. 40.

43. Hydr. bichlor. corros..... 0.1–0.2 (gr. iss.–iij.)
Spts. vini gallici..... 50.0 (ʒ iss.)
Aq. font. (dest.)..... 150.0 (ʒ ivss.)
S. Use as a wash in papular, impetiginous, and squamous lesions on the head.

44. Hydr. bichlor. corros..... 0.05–0.1 (gr. ¾–iss.)
Aq. coloniensis..... 20.0–50.0 (ʒ v.–xij.)
Aq. dest..... 100.0 (ʒ iij.)
S. Use as No. 43.

45. Acidi lactic..... 0.5–1.0 (gr. viij.–xv.)
Aq. dest..... 150.0 (ʒ ivss.)
Aq. coloniensis..... 50.0 (ʒ iss.)
S. Use as No. 43.

46. Plumb. acet..... 10.0 (ʒ iiss.)
Aq. dest..... 500.0 (O i.)
S. Use as a dressing or wash in acute dermatitis.

47. Alum. crud..... 5.0 (gr. lxxv.)
Plumb. acet..... 25.0 (ʒ vi.)
Aq. dest..... 500.0 (O i.)
S. Filter and employ as a wash or dressing like No. 46. It must be freshly prepared.

48. Acid. carbol. liquefact..... 10.0 (ʒ iiss.)
S. To be once thoroughly rubbed into any injured parts which have come in contact with infectious secretions; also used for a radical cauterization of venereal or any other stubborn ulcer.

49. Zinci chlor..... 1.0 (gr. xv.)
Aq. dest..... 5.0–10.0 (♏lxxv.–cl.)
S. Caustic to be used in phagedena and venereal ulcer.

50. Acidi carbol..... 2.0–5.0 (gr. xxx.–lxxv.)
Spts. vini..... 20.0 (ʒ v.)
S. Caustic.

51. Arg. nitratis..... 2.0–4.0 (ʒ ss.–i.)
Spts. vini (or aquæ)..... 20.0 (ʒ v.)
S. Caustic. (Alcoholic solutions frequently penetrate more deeply than watery solutions.)

52. Hydr. chlor. corros..... 2.0–5.0 (gr. xxx.–lxxv.)
Spts. vini (or aquæ)..... 20.0 (ʒ v.)
S. Caustic.

53. Hydr. chlor. corros..... 0.5–1.0 (gr. viij.–xv.)
Collodii..... 10.0 (ʒ iiss.)
S. For encrusting permanently organized papules (apply carefully, with heed to the surrounding parts).

54. Iodoform..... 2.0 (ʒ ss.)
Æther. sulph..... 20.0 (ʒ v.)
S. To be painted or sprayed on fissured ulcers.

55. Iodoli..... 2.0–5.0 (gr. xxx.–lxxv.)
Æth. sulph..... 20.0 (ʒ v.)
S. Use as No. 54.

56. Hydrarg. chlor. corros..... 0.05–0.2 (gr. ¼–iij.)
Spts. vini or æth. sulph..... 20.0 (ʒ v.)
(Or spts. vini and æther. sulph.....āā 10.0 [ʒ iiss.])
S. To be painted on syphilitic indurations of the mucous membrane and tender portions of the skin.

57. Hydr. chlor. corros..... 0.05–0.2 (gr. ¼–iij.)
Collodii,
Æth. sulph.....āā 10.0 (ʒ iiss.)
Ol. olivæ ..... 0.2 (♏ iij.)
S. Use as No. 56 and in palmar and plantar syphilides.

58. Ung. hydrargyri..... 20.0 (℥ v.)

S. A piece the size of a bean is to be rubbed in to promote the absorption of indurated lymphatic glands; for introduction into the foreskin where hidden chancres are present; also as a dressing for syphilitic ulcers.

59. Hydrargyri chlor. mitis,
Flor. zinci..... 5.0–10.0 (gr. lxxv.–cl.)
Lanolini, vaselini,
Axung. porci recent.....ää 25.0 (℥ vi.)

S. In superficial syphilitic indurations. Also used as No. 60.

60. Hydr. ammoniati..... 5.0 (gr. lxxv.)
Zinci oxidi..... 10.0 (℥ iiss.)
Axung porci. recent..... 50.0 (℥ iss.)

S. In acne and syphilitic indurations complicated with eczema.

61. Calomel..... 5.0 (gr. lxxv.)
Traumaticini..... 20.0 (℥ v.)

S. To be painted over syphilitic indurations. (The bottle should be shaken before an application is made.)

62. Iodi puri..... 0.2 (gr. iij.)
Potassii iodidi..... 2.0 (℥ ss.)
Aq. dest..... 20.0 (℥ v.)

S. Subcutaneous injections of 0.1–0.2 c.c. to be made in the neighborhood of indurated swollen lymphatic glands, epididymitis, and syphilitic infiltrations.

63 *a*. Iodoform..... 2.0 (℥ ss.)
Vaselini liquidi..... 20.0 (℥ v.)

S. Use as No. 62.

63 *b*. Plumbum causticum:
Liquoris potassæ causticæ (30 per cent.)..... 7.5 (℥ ij.)
Lythargyri..... 0.25 (gr. iv.)

S. To be applied carefully only to small and broad-based venereal papillomata, by means of a fine cotton tampon or a pointed piece of wood, or to be rubbed in until the base of the wart becomes covered with a scab on a level with the surrounding integument or somewhat below it; the part is then to be covered with a gauze bandage.

64. Acidi lact..... 5.0 (gr. lxxv.)
Æth. sulph..... 8.0 (℥ ij.)
Collodii..... 2.0 (℥ ss.)

S. To be applied to venereal papillomata once or twice a day, after the upper layers have been removed.

65. Acidi lact.,
Æth. sulph.....ää 10.0 (℥ iiss.)
Hydr. chlor. corros..... 0.1–0.3 (gr. iss.–ivss.)

S. To be painted on venereal warts.

66. Resorcini..... 8.0 (ʒ ij.)
Sacch. albi..... 1.0 (gr. xv.)
S. To be applied to venereal papillomata.

67. Resorcini..... 2.0–6.0 (ʒ ss.–iss.)
Aq. destil..... 100.0 (℥ iij.)
S. Application to venereal papillomata.

68. Sodii arseniat..... 1.0 (gr. xv.)
Aq. dest..... 100.0 (℥ iij.)
S. Dressing for venereal warts.

69. Acidi arseniosi,
Morph. muriat.....āā 0.25 (gr. iv.)
Calomel..... 2.0 (ʒ ss.)
Gummi arab. pulv..... 12.0 (ʒ iij.)
S. Use as No. 66.

70. Solutio arsenicalis alcoholica: An excess of arsenious acid is boiled in alcohol (in a retort with the cooler turned upward); after cooling, it should be set aside for a time and then filtered; at the usual temperature of the room, the solution will contain one per cent. of arsenious acid. This is to be applied, either in concentrated form or diluted with half its quantity of alcohol, once or twice a day, by means of a splinter of wood or a toothpick, to venereal papillomata.

71. Ferri sesquichlor. cryst..... 10.0 (ʒ iiss.)
Spts. vini. dil..... 10.0 (ʒ iiss.)
S. To be painted on pedunculated venereal papillomata.

72. Hydr. chlor. corros.,
Ammonii chlor. (or sodii chlor.).....āā 15.0–20.0 (ʒ iv.–v.)
Aq. fontan..... 200 0 (℥ vi.)
S. To be used in a full bath (in a wooden or porcelain bathtub) in the constitutional treatment of adults.

73. Hydrarg. chlor. corros.,
Ammonii chlor. (or sodii chlor.)..āā 1.0–5.0 (gr. xv.–lxxv.)
Aq. font..... 200.0 (℥ vi.)
S. Use as No. 72; for children.

74. Calomel..... 25.0 (ʒ vi.)
Traumaticini..... 100.0 (℥ iij.)
S. A portion of the body to be painted with this every three to eight days; for use in constitutional treatment. (The bottle must be shaken before using.)

75. Ung. hydrargyri, 1.0–2.0–5.0 (gr. xv.–xxx.–lxxv.) or more.
S. 10, 20, 40, or more doses of this size should be prescribed in waxed paper or capsules. One of these to be rubbed in every other day, every day, or morning and evening, by turns; as a constitutional treatment.

76. Ung. hydrarg..... 0.2–1.0 (gr. iij.–xv.)
S Use as No. 75, in the case of children.

77. Unguentum cinereum lanolinatum forte:
Lanolini anhydrici..... 15.0 (ʒiv.)
Chloroformi..... 50.0 (℥iss.)
Evaporate in a large mortar, with continual stirring, down to 30.0.
Then add:
Hydrarg. vivi depur..... 30.0 (℥i.)
Stir slowly until the chloroform is wholly evaporated and the metallic mercury can no longer be distinguished.

78. Unguent. ciner. lanolinat. fortis (No. 77)... 9.0 (gr. cxxxv.)
Ol. vaselini..... 3.0 (gr. xlv.)
Add the oil to the ointment very gradually with constant stirring until a smooth, oily mixture is obtained. Keep in a wide-mouthed phial with glass stopper.
Signa: Oleum cinereum, 50 per cent.

The dose for injection of this preparation which I generally employ is 0.05 c.c., and contains 0.04 gm. of metallic mercury. Should we desire to inject in one dose double the amount of gray oil, say 0.1 c.c., two injections should be made, each of 0.05 c.c. For the constitutional treatment a dose of 0.05 c.c. is injected deeply under the skin of the back every 3 to 5 days, and when the symptoms have markedly improved, every 5 to 8 days, and the same amount, as an extra dose, is given once in 7, 14, or 21 days, in all 8 to 12 times, rarely more. In early relapses one-half the quantity is frequently sufficient. For local treatment 0.01 c.c. is to be injected (at the border of the induration, and deeply under the skin); in scleradenitis inguinalis a dose (0.05 c.c.) is injected deeply in the neighborhood of the abdomen, 3–4 cm. about Poupart's ligament.

79. Ung. ciner. lanolinat. fortis (No. 77).... 4.5 (gr. lxviiss.)
Ol. vaselini..... 5.5 (gr. lxxxiiss.)
S. To be prepared as in No. 78.
Signa: Oleum cinereum 30 per cent. (0.1 c.c. contains 0.0366 gm. of mercury). Double the quantity to be used (0.1 c.c. at a dose) than of No. 78.

80. Ung. ciner. lanolinat. fort. (No. 77),
Lanolini.....āā 3.0 (gr. xlv.)
Paraffin. liquidi..... 4.0 (ʒi.)
Signa: Oleum cinereum 20 per cent. (1 c.c. contains 0.22 gm. of mercury). To be injected deeply under the skin in doses of 0.05 c.c = 0.01 gm. of metallic mercury. Used in the constitutional treatment of children.

81. Calomel,
Ol. vaselini.....āā 4.5 (gr. lxviiss.)
Lanolini..... 4.0 (gr. lx.)
(One cubic centimetre contains 0.371 gm. of mercury.) To be used the same as No. 79 for constitutional treatment.

82. Hydr. oxid. flav..... 4.0 (gr. lx.)
Ol. vaselini..... 4.5 (gr. lxviiss.)
Lanolini..... 3.5 (gr. xlv.)
(One cubic centimetre contains 0.392 gm. of mercury.) S. Use as No. 81.

83. Hydrarg. salicyl..... 7.0 (gr. cv.)
Ol. vaselini..... 4.0 (♏ lx.)
Lanolini..... 2.0 (gr. xxx.)
(One cubic centimetre contains 0.422 gm. of mercury.) S. Use as No. 81.

84. Hydrarg. oxid. nigr..... 4.7 (gr. lxxss.)
Ol. vaselini..... 6.2 (♏ xciij.)
Lanolini..... 3.1 (xlviss.)
(One cubic centimetre contains 0.39 gm. of mercury.) S. Use as No. 81.

85. Hydrarg. thymoloacet..... 7.0 (gr. cv.)
Ol. vaselini..... 5.0 (♏ lxxv.)
Lanolini..... 2.5 (gr. xxxviiss.)
(One cubic centimetre contains 0.36 gm. of mercury.) S. Use as No. 81.

86. Hydr. carbolatis..... 7.0 (gr. cv.)
Ol. vaselini..... 4.0 (♏ lx.)
Lanolini..... 2.0 (gr. xxx.)
(One cubic centimetre contains 0.375 gm. of mercury.) S. Use as No. 81.

87. Hydrargyr. sozoiodol..... 0.8 (gr. xij.)
Potassii iodidi..... 1.6 (gr. xxiv.)
Aq. destil..... 10.0 (℥ iiss.)
S. One subcutaneous injection to be made weekly (1 c.c. of the solution); used in constitutional treatment.

88. Hydr. chlor. corros..... 0.2 (gr. iij.)
Sodii chlor..... 2.0 (℥ ss.)
Aq. dest..... 20.0 (℥ v.)
S. One cubic centimetre of the solution to be injected daily; used in constitutional treatment.

89. Hydrarg. chlor. corros..... 0.6 (gr. ix.)
Sodii chlor..... 6.0 (℥ iss.)
Aq. dest..... 20.0 (℥ v.)
S. One cubic centimetre of the solution to be injected every third or fourth day, when the symptoms improve every fifth to eighth day; used in the constitutional treatment.

90. Hydr. formamid..... 0.2–0.4 (gr. iij.–vi.)
Aq. dest..... 20.0 (℥ v.)
Keep in a dark glass bottle. S. One syringeful (1 c.c.) to be injected daily or every second day. Use as No. 88.

91. Hydr. succinimid.,
Cocainæ muriat.....āā 0.2 (gr. iij.)
Aq. dest..... 20.0 (℥ v.)
S. One cubic centimetre to be daily injected subcutaneously. Used in constitutional treatment.

92. Unguent. hydrarg. lanolinati (50%). 6.0 (℥ iss.)
Extr. opii aquos..... 0.5–1.0 (gr. viiss.–xv.)
Sacch. lactis..... 14.0 (℥ iiiss.)
S. Make 120 pills; 3, 6, or 9 to be taken daily (it is well to increase by 1 pill every second day).

93. Hydr. tannatis..... 0.1 (gr. iss.)
(Opii pulv..... 0.01 = gr. ⅙)
Sacch. lactis..... 0.4 (gr. vi.)
S. Two to three such doses to be taken daily in wafers.

94. Hydr. tannatis..... 2.50 (gr. xxxviiss.)
Extr. opii..... 0.25 (gr. iiss.)
Lanolini..... 1.25 (gr. xviiss.)
Sacch. lactis..... 3.75 (gr. lviss.)
Make 50 pills. S. Four to six to be taken daily.

95. Hydr. tannatis..... 0.2 (gr. iij.)
Sacch. lact..... 5.0 (gr. lxxv.)
Divide into 10 powders. S. Use as No. 93; for children.

96. Calomel..... 0.5 (gr. viiss.)
(Opii..... 0.05 = ⅙)
Sacch. albi..... 5.0 (gr. lxxv.)
Divide into 10 powders. S. Two or three to be taken daily.

97. Calomel..... 0.2 (gr. iij.)
Sacch. albi..... 10.0 (ʒ iiss.)
Divide into 20 powders. S. Use as No. 95.

98. Calomel..... 0.2 (gr. iij.)
Ferri lact..... 0.4 (gr. vi.)
Sacch. lact..... 10.0 (ʒ iiss.)
Divide into 20 powders. S. Use as No. 95.

99. Calomel..... 2.50 (gr. xxxviiss.)
Extr. opii..... 0.25 (gr. iiss.)
Lanolini..... 1.50 (gr. xxiiss.)
Sacch. lact..... 3.75 (gr. lviss.)
Make 50 pills. S. Two to five to be taken daily.

100. Hydrarg. iod. virid..... 1.5 (gr. xxiiss.)
Extr. opii aq..... 0.5 (gr. viiss.)
Lanolini..... 1.5 (gr. xxiiss.)
Sacch. lactis..... 4.5 (gr. lxviiss.)
Make 50 pills. S. Use as No. 99.

101. Hydr. chlor. corros..... 0.25 (gr. iiiss.)
Dissolve in a very little ether and add:
Lanolini..... 1.50 (gr. xxiiss.)
Sacch. lact..... 3.75 (gr. lviss.)
Extr. opii aq..... 0.50 (gr. viiss.)
Make 50 pills. S. One to three to be taken daily.

102. Hydr. chlor. corros..... 0.1 (gr. iss.)
Aq. dest. (font.)..... 200.0 (ʒ vi.)
S. One to three tablespoonfuls to be taken daily in half a glass of water, milk, sweetened water, beer, etc.

103. Hydr. chlor. corros..... 0.1 (gr. iss.)
Spts. vini rectif..... 15.0 (ʒ ss.)
Aq. fontan. (dest.)..... 150.0 (ʒ v.)
S. One to three tablespoonfuls to be taken daily in a glass of water.

104. Hydr. chlor. corros..... 0.1 (gr. iss.)
Spts. sacchari..... 100.0 (ʒ iij.)
S. Half a tablespoonful (10 gm.) to be taken in tea once to three times daily.

105. Potass. iodidi (sodii iodidi or rubidii iodidi)..... 5.0–10.0 (gr. lxxv.–cl.)
Aq. font. (dest.)..... 200.0 (ʒ vi.)
S. One to three tablespoonfuls (20 gm.) to be taken daily in half a glass of water, milk, sugar and water, beer, etc. (In some persons the iodine salts cause constipation, in others diarrhœa; a corresponding amount of syrup of manna or of diacodion should then be added.)

106. Potassii iodidi (sodii iodidi or rubidii iodidi)..... 0.5–2.0 (gr. viiss.–xxx.)
Aq. fontan..... 100.0 (ʒ iij.)
S. Two to three teaspoonfuls to be administered daily; for children.

107. Potassii (sodii or rubidii) iodidi..... 2.0–20.0 (ʒ ss.–v.)
Divide into 4 powders and fold in waxed papers. S. One powder to be taken during the day in two or three portions; dissolved in milk or water.

108. Potassii (sodii or rubidii) iodidi... 0.5–2.0 (gr. viiss.–xxx.)
Divide into 5 powders. S. Use as No. 107; for children.

109. Potassii (sodii) iodidi..... 10.0 (ʒ iiss.)
Aq. font..... 200.0 (ʒ vi.)
Extr. belladonnæ..... 0.1–0.15 (gr. iss.–ij.)
S. Use as No. 105 (when a tendency to iodism is present).

110. Tinct. iodi..... 2.0 (ʒ ss.)
Aq. font. (dest.)..... 200.0 (ʒ vi.)
S. One to three tablespoonfuls to be taken daily.

111. Potassi iodidi..... 10.0 (gr. cl.)
Sacch. lact..... 5.0 (gr. lxxv.)
Lanolini..... 3.0 (gr. xlv.)
Make 50 pills. S. Two to ten to be taken daily.

112. Potassii iodidi..... 1.0–4.0 (gr. xv.–lx.)
Aq. font. (lactis)..... 100.0–200.0 (ʒ iij.–vi.)
S. Use as a clysma in rectal medication.

113. Potassii iodidi,
Aq. destil.....ää 5.0 (gr. lxxv.)
Codeinæ..... 0.05–0.1 (gr. ¾–iss.)
S. One to three cubic centimetres to be injected subcutaneously daily.

114. Iodoli ..... 10.0 (ʒ iiss.)
Divide into 20 doses. S. Two to six to be taken daily in wafers.

115. Iodoformi ..... 10.0 (gr. cl.)
Sacch. lact. ..... 5.0 (gr. lxxv.)
Lanolini ..... 2.0 (gr. xxx.)
Make 50 pills, and keep in a phial with glass stoppers. S. Five, ten, or twelve to be taken daily.

116. Pilulæ Blancardi (ferri iodidi) ..... No. 50.
S. Three to six to be taken daily.

117. Ferri pulverati ..... 2.0 (gr. xxx.)
Iodi ..... 4.0 (gr. lx.)
Sacch. ..... 3.5 (gr. liiss.)
Pulv. rad. glycyrrhizæ ..... 7.0 (gr. cv.)
Aq. dest. ..... 2.5 (♏ xxxviiss.)
Make 100 pills. S. Use as No. 116.

118. Syr. ferri iodidi ..... 1.0–5.0 (gr. xv.–lxxv.)
Syr. mori (simplicis) ..... 20.0 (ʒ v.)
S. To be taken in the course of a day. (To be freshly prepared each day.)

119. Iodi puri ..... 0.1 (gr. iss.)
Ol. morrhuæ ..... 100.0 (ʒ iij.)
S. One to two tea- or tablespoonfuls to be taken daily in the case of anæmic or scrofulous individuals.

120. Antipyrini ..... 2.0–5.0 (gr. xxx.–lxxv.)
Potassii iodidi ..... 5.0–10.0 (gr. lxxv.–cl.)
Aq. font. (dest.) ..... 200.0 (ʒ vi.)
S. Use as No. 109.

121. Antipyrini ..... 5.0–10.0 (gr. lxxv.–cl.)
Divide into 10 powders. S. One to three powders to be taken daily (in the evening) for headache.

122. Radicis sarsaparillæ ..... 300.0 (ʒ ix.)
After maceration for two hours with aq. font. 2000.0 (O iv.) boil down to 150–200 (ʒ ivss.–vi.). Strain and add
Saccharini ..... 0.01 (gr. ¼)
Or
Glycerini or syr. simplicis ..... 10.0 (ʒ iiss.)
S. Two to three tablespoonfuls to be taken daily. In the case of children as many teaspoonfuls.

123. Liq. sodii arsenit.,
Aq. aurantii flor. ..... āā 5.0 (gr. lxxv.)
S. Dose, 5 drops increasing to 30 and over, daily, in anæmia and neuroses.

124. Liq. sodii arsenit. ..... 5.0 (gr. lxxv.)
Tinct. ferri malatis ..... 20.0 (ʒ v.)
Aq. dest. ..... 150.0 (ʒ ivss.)
S. One to two tablespoonfuls to be taken daily, in anæmic conditions.

125. Acidi arseniosi ..... 0.5 (gr. viiss.)
(Extr. opii aq ..... 0.1) (gr. iss.)
Sacch. actis..... 6.5 (gr. xcviiss.)
Lanolini ..... 8.0 (gr. xlv.)

Make 100 pills. S. Three, ten, or fifteen (gradually increasing) to be taken daily; in anæmic individuals.

126. Aq. Roncegno (Levico).

S. Anæmic individuals should take about three tablespoonfuls immediately before or after each meal.

127. Aq. Guber.

S. Use as No. 126.

INHERITED SYPHILIS.

BY

JONATHAN HUTCHINSON,

LONDON.

INHERITED SYPHILIS.

It is now universally admitted that syphilis may be transmitted from parent to offspring. This was denied by some of the leading surgeons of the last century, and even in our own times it has been strongly asserted that such transmission can occur only through the mother. The conviction that the father as well as the mother may transmit it has, however, steadily gained ground. The present creed, and I have no doubt the correct one, is that by far the most common transmission is from the father. We do not know anything for certain as to whether the disease receives modifications in connection with its descent from one or other parent or from both, but an opinion prevails that if the mother has syphilis the risk to her offspring is greater than if the taint be on the paternal side only. Many women married to husbands who have had syphilis bear tainted children, yet remain themselves apparently free. It is also well known that a majority of the children destined to suffer from inherited taint appear to have enjoyed perfect health during intrauterine life and are at the time of birth well grown and free from blemish. Such facts justify the inference that when the mother is herself diseased a greatly increased risk to the health of her fœtus must be introduced. It is sufficient to mention the possible occurrence of specific disease of the placenta to illustrate this point. It is at the same time very possible that this increase of risk is chiefly manifested during intrauterine life, and that if the child be born apparently free its subsequent liabilities may be much or quite the same whether it has inherited from father, mother, or both.

Syphilis and Abortion.—There is no reason whatever to believe that the existence of syphilis in either sex operates in any way to prevent conception. Cases are abundant in which large families are born to parents both of whom have suffered from this disease. It may be plausibly asserted that the popular creed which assigns to syphilis a foremost place as a cause of abortion is greatly based on exaggeration. Abortions for which no cause can be assigned, and often occurring in long succession to the same mother, are very common not only in the human family, but among the domestic animals. It is very

probable that in many instances in which they happen to syphilitic parents the relation is merely one of coincidence. In saying this, however, it is by no means intended to deny that syphilitic disease of the placenta and possibly other pathological events may determine the death of the fœtus. We have, however, the unquestionable fact that in a great number of instances, even when the disease has been quite recently acquired by one or both parents, the pregnancy may yet proceed favorably, and a well-grown but tainted child be produced at term.

Period during which Syphilis is Transmissible.—It is, I think, very probable that in women who have suffered from acquired syphilis the liability to transmit to offspring lasts much longer than it does in men. A large experience on this point has led to the conclusion that a man very rarely becomes the father of a syphilitic child if an interval of two years has elapsed since his disease was acquired. In the majority of cases a much shorter interval is probably sufficient, but two years appears to be long enough almost without regard to the treatment adopted. It is possible that now and then an exception may occur, but I feel sure that this statement expresses the general fact. Our data as regards women are far less abundant and in most instances much more open to question. It is almost certain, however, that in some instances married women have—without any reinforcement of the taint—continued to bear syphilitic children through a succession of five, seven, or even ten years. It is possible that these very exceptional cases may come under the law of telegony and that more than one ovum may have received the virus at the date of the first conception. I know of no parallel cases as regards length of time in the male sex.

Facts which I cannot but think are very strong in favor of the belief that the period during which a parent can produce a syphilitic child is in most instances limited will be found in a work on "Diseases of the Eye and Ear in Connection with Inherited Taint," published by me in 1864. They are not the less convincing because they were collected and tabulated without any reference to the point in question and at a time when my opinions were much less definite than they are at present. As the result of the analysis of eighty-two cases of interstitial keratitis it is there shown that in two out of every three cases the patient was the eldest in the family. It was further shown that the average number of children which had survived in seventy-seven instances in which the mother had borne one syphilitic child was 3.4. Now, had all these children been equally liable to suffer, the proportion in which the eldest was the victim ought to have been two in seven instead of two in three. The suggestion is obvious that the

younger members of syphilitic families usually escape all taint, and the facts would be yet stronger if the cases were excluded in which the disease was acquired by the parent subsequent to the birth of some of the children.

Colles's Law.—The question as to whether a woman who bears to a syphilitic husband a tainted child herself receives any form of infection has been much debated. Unquestionably she remains in most instances apparently quite well, and proof is yet wanting that she ever manifests either during her pregnancy or afterwards any acute and definite outbreak of secondary symptoms. In all cases in which these occur there has probably been a primary sore. On the other hand, there is a certain amount of evidence that such women do not infrequently show certain vague symptoms of the tertiary class and that they are to a large extent immune as regards subsequent infection. Colles made the observation—since exalted into what is called Colles's law—that syphilitic children with sore mouths, whilst very prone to infect the nipples of wetnurses, might be nursed by their own mothers with impunity. A few exceptions to this observation have now been recorded, and also a few other cases bearing in the same direction in which women who have borne syphilitic children have subsequently contracted primary syphilis from other sources. We must admit then that mothers of this class do not invariably acquire immunity, but at the same time we must remember that there are those to whom syphilis even in its primary and secondary forms appears to afford but very short protection from another attack. I have more than once known a man to contract a second well-characterized chancre within a year of the first and before his symptoms had entirely ceased. My own experience does not supply me with a single exception to Colles's law. I have often seen chancres which had been contracted by nurses from syphilitic infants, but I never saw one in a mother of such. When we remember that the number of syphilitic mothers who suckle their infants is to be counted by thousands and that of wetnurses only by tens, we can feel no doubt that Colles's observation was in accordance with fact. It follows then that the mother of a syphilitic infant does, at any rate in the majority of instances, receive from the fœtus in her womb some influence which confers a large measure of immunity. Does such influence at the same time render her liable to taint the result of future conceptions? On this point our facts are not conclusive. In a majority, perhaps a very large one, there is reason to think that no such liability is incurred. If it were, the disease would start *de novo* from the mother, and her second child would probably be more liable to suffer than her first. Her family would in the future inherit from herself, even if by lapse of time the taint

had died out in her husband. It may be that in some cases this does really happen, but our facts bear strongly in the opposite direction. In most cases when syphilis is inherited it is the eldest child which suffers most, and often it is the first-born only. I have made much use of this fact and have cited much evidence in its proof in the work above mentioned.

As regards the practical question whether or not the mother of a syphilitic infant should be allowed to suckle it, I cannot but think that it should be answered in the interest of the child in the affirmative. The risk to the mother is probably infinitesimal, and the gain to the child under most circumstances is great. If, however, the question be raised, it must be admitted candidly that risk is not absolutely excluded, although, as stated above, I have yet to see an exception to Colles's law. Mr. Lockwood, in his report on syphilis as treated in St. Bartholomew's Hospital, contained in volume 33 of the Reports, records a case in which the mother of a syphilitic infant had what was supposed to be a chancre of the nipple with enlargement of the axillary glands. Careful examination, however, revealed the existence of the scar of a chancre on one labium with enlarged inguinal glands. It thus became probable that the sore on the nipple was the result of irritation and not of primary specific infection. Had the case fallen under the observation of one eagerly in quest of exceptions to Colles's law, it might easily have been made to tell a different story. The question as to the degree of immunity afforded to the mother by a syphilitic pregnancy may possibly be in some relation to what happens to the fœtus itself.

Fœtal Syphilis.

As already stated, in many instances the fœtus during intrauterine life maintains a good state of health, and it is only after birth and after a certain period of independent life that it begins to manifest evidences of taint. Nothing is more common than for an infant in whom the taint has exhibited itself with severity to be declared to have shown at birth every sign of health. Usually it is about at the end of a month or six weeks from birth that snuffles and a dusky erythema about the neck and genitals soon followed by wasting attract attention. This delay is not, however, the absolute rule. Macerated fœtuses which have died in utero are now and then produced, showing evidence of having suffered from syphilitic symptoms, and, which is perhaps yet more conclusive, infants are sometimes born alive with all the usual signs of taint already present. (See a lecture by Parrot, "La syphilide bulleuse," in *Le Progrès Médical*, January

26th, 1878.) When this occurs it is perhaps almost invariable that death follows in a few days. On this point, however, I speak from the knowledge of but a very small number of observed facts.

There is also a peculiar disease known as *pemphigus neonatorum* which usually shows itself by bullæ on the hands and feet and which appears within a few days of birth and almost always ends fatally. Cases of survival have, however, been reported in the *British Medical Journal* of January 21st, 1882, and in *The Archives of Surgery*, Vol. IX., p. 12. This disease, like most of the syphilitic manifestations, has its analogue or prototype in a family form of infantile pemphigus of the extremities, which also begins within a few days of birth, but which, although very severe, does not end fatally. These facts prove incontestably that the virus of syphilis may develop in the blood and tissues of the unborn infant, and they also leave us the difficult problem as why it should do so in some instances and not in all. Future observation may possibly throw light on this question; for the present we have little or none.

To Parrot we owe the statement that he has seen many cases of syphilitic pemphigus in infants and has made many autopsies with the result that he has never found any lesions of the viscera. Thus it becomes yet more difficult to explain why it should be—as it almost invariably is—a fatal manifestation.

Visceral Affections.—Although, however, we may accept M. Parrot's experience, confirmed as it is by that of many others, as indicating that visceral affections are not common in intrauterine syphilis, there can yet be no doubt that they do occasionally occur. Amongst these, a *parenchymatous infiltration (fibroplastic) of the liver*, for the most part without large gummata, is the most common (Bärensprung, Gubler, Rochebronne, and others). It is sometimes attended by anasarca and by similar lesions in the lung. If not actually present at birth, it may be developed soon afterwards, and may then lead to jaundice and death. Infiltrations of the same kind may be found also in the *spleen*, the *kidneys*, the *thymus*, and even in the *heart*. Occasionally larger and more circumscribed deposits are found, and sometimes softening occurs and abscesses form. Lecount, Mracek, and others have published isolated examples of gummata present in the substance of the heart at the time of birth.

The pathological processes just adverted to occur chiefly during the later period of intrauterine life and are no doubt responsible for the majority of cases in which the child is born dead at or near full time. They may occur also during the first few weeks of life. At this age *jaundice* is sometimes observed and is a symptom indicative of great danger.

It may probably be accepted as a rule that if syphilitic manifestations occur during intrauterine life or immediately after birth the malady is likely to prove very severe. The number of infants affected at these periods who survive is not large. The older the child at the date of the first symptoms the more likely it is that it will bear the disease and prosper under the treatment.

I cannot find in the perusal of the case narratives of these early and severe forms that there is any good reason for associating them with special forms of the disease in the parent. In most cases, probably, the mother had suffered, but in many there was no proof of this, and in more than a few it is expressly stated that she denied all disease and appeared to be in good health. It may be noted that these early forms usually occur in first pregnancies. The reader will find an important series of cases illustrating these statements narrated by De Rochebronne in a thesis published in 1874.

Secondary Symptoms.

Although, as we have seen, the virus of syphilis when present in the ovum may show its effects at any stage of fœtal life, yet we must repeat that it is undoubtedly a very common result that it manifests no apparent influence until some weeks after birth. The child is born to all appearance quite sound, but on reaching the age of from one to three months it becomes the subject of a whole group of phenomena of the secondary class. It will be observed with interest that this is just about the same length of time which in the acquired disease intervenes between the acquisition and the secondary outbreak. Nor are the symptoms which show themselves very dissimilar. We do not encounter pemphigus or any very exceptional form of dermatitis. An erythematous, papular, or scaly eruption is the common form, and there are sores on the lips, condylomata at the anus, pains in the bones, with slight and transitory forms of periostitis, just as in the acquired disease. To complete the parallel we occasionally see iritis, and this form of eye disease occurs only at this stage and with precisely the same concomitants as in the acquired malady.

If mercurial treatment be promptly resorted to and judiciously carried out, the disease in infants of this age is usually subdued and good health is restored. Nor do the secondary phenomena as a rule return. It is even probable that in many cases without specific treatment recovery takes place and all the conditions are in their nature—like those of the acquired disease—transitory. Although, however, this may be the rule, it is not without many exceptions, and nothing can perhaps be mentioned as a possibility in the secondary stage of the

acquired disease which may not happen in this. It is to be noted also that during this stage the blood and all inflammatory secretions from the patient's tissues are very contagious.

It is from patients in this stage and very mildly affected that the transference of *syphilis by vaccination*—sometimes to twenty persons from the lymph of one vesicle—has occurred. The vaccinifers in these cases have usually at the time appeared to be in good health. This fact leads to the remark that it is probable that in some cases in which the child inherits even a very potent virus all obvious indications of it in infancy and possibly throughout life may be absent. This fact is exceedingly important, and it is again not without its parallel in the acquired form of the disease. Although probably in a large majority of cases in which infants exhibit the phenomena of the secondary stage of syphilis in the second or third month of life, those phenomena disappear in the course of a few weeks or months and leave the child apparently restored to health, this is not invariable. Various complications may arise, and to these it may be convenient to advert seriatim.

The *skin eruption* may be very severe and extensive and may induce much wasting and cachexia. Not infrequently the infant remains plump and strong through the whole course of the disease, but in many cases it is otherwise, and a shrivelled state of emaciation results in which the patient acquires a withered, old-man-like facies. In this state, complicated perhaps by diarrhœa and convulsions, death may occur.

The various *viscera* may be affected after the manner which has been already described as occurring in the cases in which the symptoms appear earlier. Visceral affections are, however, decidedly exceptional in these cases.

The *osseous system* may suffer. Probably in all forms of secondary syphilis there is a liability to general periostitis, usually of a slight and transitory form. The bones become tender, there is slight enlargement, and what are called osteocopic pains result. In the cases under discussion this general periostitis may be severe, but it is still transitory. The skull bones may be affected and the encrustations produced which are known as Parrot's bosses, or the long bones near to the epiphyses may suffer and a simulation of local paralysis result. Now and then suppuration may occur. Periostitis near the joints often simulates joint disease, and as the bone is at this age in rapid growth an inflammation at an epiphyseal end, although itself transitory, may cause permanent deformity.

The *nervous system* may suffer in various ways. There may be a slight and transitory meningitis leading to a degree of hydrocephalus.

It is not, however, easy to specify any definite forms of nervous lesion which have been proved to occur at this stage.

It may be assumed to be probable that the *vascular system* suffers less in inherited syphilis than it does in the parallel stage of the acquired form, for subsequent degenerations in connection with it are far less common.

The *eye*, as has been said, may be attacked by acute iritis. Nodules of rust-colored lymph are effused, and the conditions generally are exactly like those in the acquired form. The pupil may be blotched unless atropine be used early. I have collected a series of twenty-two cases of acute iritis in connection with this form of syphilis (see *Clinical Memoirs*, 1863, p. 18). From this series it appeared that the age of five months is that at which iritis usually occurs, that the infants often appear to be in good health, that the period since the parental disease has usually been short, and that female children suffer more frequently than males in the proportion of three to one.

The *larynx* (Barlow) and the *testes* (Carpenter) are amongst the organs which may in exceptional cases suffer in this state of congenital syphilis.

Diagnosis.

The diagnostic recognition of inherited syphilis is a matter of much difficulty at all stages of the malady, and the belief that it is easy leads to constant errors. Single symptoms, however apparently characteristic, are but seldom trustworthy. In infancy the group made up by snuffling respiration, a ham-colored erythema affecting the neck, face, extremities, and genitals, a general wasting, and a senile physiognomy may often be so marked as to leave no room for hesitation. They must, however, be taken together, for no one of them when alone is of much value. Snuffles is after all often merely a matter of degree, and many infants suffering from coryza may be thought to snuffle more or less. So also some conditions of infantile eczema may closely simulate syphilitic eruptions. The atrophy is seldom characteristic and may occur in connection with many other causes of debility. The symptoms mentioned must therefore be taken together and judged with caution, and if the history is in contradiction the utmost care should be used in expressing an opinion.

The diagnosis at the secondary stage is usually easy, but sometimes exceedingly difficult. In many cases it is the surgeon's duty to exercise extreme caution in the expression of his opinion. Especially if it be known that one or other parent has suffered from syphilis is there danger of a hasty conclusion. I feel sure that under

such circumstances the inherited taint is often erroneously held to be proved not only by the parent, but by his medical advisers. There are some single symptoms which, if well characterized, are conclusive; such, for instance, is a condyloma, and perhaps also iritis. The eruption may easily mislead, and those who trust to the "coppery tint" of an erythematous congestion are very likely to go wrong. The symptom of snuffles is very valuable if well pronounced and persistent; otherwise not in the least so. It is, however, to the combination of a group of symptoms—a dusky scaly eruption, troublesome snuffles, sores at the angles of the mouth, etc.—that we must usually trust. Infants are liable to forms of eczema which may easily be mistaken for syphilis, as also may those which sometimes follow vaccination.

Treatment.

The treatment of secondary syphilis in the infant is by the cautious use of mercury. Inunction with a diluted mercurial ointment is probably the best plan. This method of treatment is not, however, without its disadvantages and its dangers. It is certain that mercury at this age is very prone to cause damage to the enamel of the permanent set of teeth. It is as yet uncertain whether it tends to prevent the attacks of keratitis, otitis, and other affections incident to the period of puberty and afterward. If, therefore, an infant known to be the subject of inherited taint is free from symptoms and apparently thriving, it may be an open question whether it is wise to use mercury. On the whole, however, it is perhaps better to do so.

Tertiary Symptoms.

After the secondary stage of inherited syphilis has been passed and all symptoms have disappeared (which will usually be at the end of six months, and almost invariably by the end of twelve), there will follow an interval of years during which the patient appears quite well. All risk of the infection of others has now ceased. After an interval varying much in length in different cases other phenomena may occur. Some of these may be definitely classed as tertiary, but about some others there is doubt.

The chronic forms of lupoid skin disease, which are so common as a tertiary symptom in acquired syphilis, are seldom or never encountered in the subjects of the inherited taint.

Influence of Sex.—It would appear that there is some disproportion of the sexes in all the later forms of disease due to inherited syphilis. In my work on syphilitic affections of the eye and ear

I collected a series of cases which appeared to show that of the subjects of infantile iritis in 23 cases 18 were females; of those of keratitis, in 102 cases 64 were females; whilst in 21 of deafness, 15 were females. If we take the total of these we find that females suffer in the proportion of more than two to one (97 females and 47 males). It is difficult to explain this unless it be that male infants suffering from congenital syphilis are more prone to die than females and that thus a larger proportion of the latter are left to encounter the later affections.

Affections of the Eyes.

Keratitis.—Amongst the most interesting of the facts which have been established as to the liabilities of those who have inherited syphilis is that they are prone to a peculiar form of inflammation of the cornea. Ophthalmic surgeons had for long been accustomed to describe under the name of scrofulous corneitis a very peculiar form of keratitis which usually affected both eyes and which was of only transitory duration and usually cleared away completely. The older atlases all contain plates illustrating this malady, and the term "ground-glass" as applicable to its early stages was well recognized. That the disease stood apart from all other affections of this structure was well known. At the present time I believe it may be said that all competent observers accept this peculiar form of interstitial keratitis, when well characterized, as in itself proof that its subject is the subject also of inherited syphilis. In itself it now constitutes a most valuable revealing symptom and has helped us to much additional knowledge respecting the later stages of the disease.

This form of keratitis does not occur in infancy and is not one of the secondary phenomena usually met with at that age. It usually waits till the patient is near adolescence or even well into adult life before it shows itself, and then it usually occurs alone—that is, unattended by any other manifestations of the taint. Its subjects have often enjoyed many years of excellent health and of the most absolute immunity from all suspicious symptoms, when suddenly both eyes become inflamed. Some of the most severe attacks are met with under these conditions. As a rule the keratitis lasts a few months and then passes away without any tendency to relapse. Its course in adolescents and adults is usually in these respects very regular, but when the disease occurs in younger children it may be somewhat less so.

The subjects of this form of keratitis very usually display peculiarities in physiognomy which support the diagnosis, and more especially is it very common for them to show a peculiar *malformation of the upper incisor teeth.* This consists in the presence of single

vertical notches in their edges which, whilst themselves evidence of the atrophy of the middle tenticle, are often attended by a general dwarfing of the whole tooth, which is both too short and too narrow from side to side. In many cases this peculiar dwarfing and the central notch are sufficiently well marked to justify a diagnosis in themselves, but in many others they amount only to a suspicious condition and require corroboration by other facts. Such corroboration may be afforded by the physiognomy, by the keratitis, by deafness, or by the parental history. Neither the presence nor the absence of the latter must, however, be allowed much weight in doubtful cases, for it may be denied when a reality and confessed when it has had no share in the production of the keratitis.

It may here be stated that there is much doubt as to whether this form of keratitis, although occurring so long after the secondary or infantile stage, ought to be allowed to rank as a tertiary manifestation. It is almost invariably symmetrical, and it is always transitory—features in which it presents marked dissimilarity from all that we know of tertiary phenomena. Its homologue also, which occurs in cases of acquired syphilis, is always amongst the secondary group. No such thing as interstitial keratitis is ever observed in the tertiary stage of the acquired disease, but a few definite ones have been witnessed in the secondary stage. I have myself seen several, but only one which was really well characterized. This was a case recorded by Morton in the Ophthalmic Hospital Reports. The problem placed before us by these facts is one of great importance, but which the present stage of our knowledge scarcely enables us to approach.

The interstitial keratitis of inherited syphilis observes several well-marked stages. In its beginning the eyes are irritable and watery, and the corneæ present patches or clouds of haze. These latter rapidly increase until the whole cornea is in a condition of partial opacity resembling ground glass. With this goes a very definite congestion of the ciliary region and to some extent of the conjunctiva also, but the comparative absence of conjunctival implication is always a marked feature. Even in the early stage there may be present on the corneal surface near the margin small crescentic patches of congestion of a salmon tint and abruptly margined. These in rare instances may spread over the whole cornea and may give it a deep plum tint of purple redness. When the cornea is in this condition, it contrasts most strongly with the comparatively pale conjunctiva which surrounds it.

When the keratitis is at its height there is usually much photophobia, and the patient is reduced to a state of practical blindness. Not infrequently, and more especially, I think, in the subjects of

inherited gout, inflammation of the knee-joints occurs coincidently with the keratitis and subsides with it. The bond of connection between the two may possibly be that of infection from inflamed tissues of similar structure, the one supplying elements which are carried to the other. Clement Lucas has recorded the observation, well confirmed by others, that in the purulent ophthalmia of infants the joints may be affected, more especially the knees.

The third stage of the disease is that of decline, all the phenomena of inflammation slowly passing away. Now occurs the most remarkable illustration of the possibilities of reparation, for a cornea which had been rendered wholly opaque and which by the uninitiated might have been deemed beyond hope of restoration may acquire again almost perfect transparency. The process of clearing may be complete in a few months or may require years. It cannot be said that it is quite invariable. I have recorded one or two cases in which the cornea remained opaque and misshapen, and the patient was almost blind, but they are extremely rare.

The keratitis here described may be attended by *iritis* and by implication of the deeper structures—retina, choroid, etc. As a rule, however, the cornea suffers almost alone. Iritis if present is never severe, and in most cases when the cornea clears the restoration of vision is almost perfect. In this the contrast with the results of iritis occurring in the secondary stage is most definite, for in the latter the pupil is usually blocked at an early period.

A condition of the retina closely simulating *retinitis pigmentosa* and one of the choroid simulating *choroiditis disseminata* are not infrequently observed in the subjects of inherited taint. The early stages, however, scarcely ever come under observation, and we may assume that they are very insidious. Not improbably the peripheral parts of the eyeball suffer more or less in most cases of severe keratitis. Some authorities hold that the keratitis is secondary to choroidal disease. The discovery of choroidal changes is often of great use in diagnosis. Although in themselves probably stationary, they are usually of no great importance.

Deafness.

A form of deafness peculiar to those who inherit syphilis frequently occurs either just before or just after the attack of keratitis. Its onset is usually rather rapid, but insidious in the sense that it is not attended by other symptoms. There is no pain and usually not much giddiness or other subjective phenomena. Loss of hearing is almost the sole symptom, but it may advance so rapidly that in the

course of a month or six weeks the patient may have become quite deaf. The pathology of the affection is probably inflammation of the delicate membrane intervening between the bone and nerve structures of the internal ear.

In this affection the most prompt and vigorous treatment is called for. Although it may be the case that, as in the keratitis, there is ultimately a spontaneous subsidence of the disease, yet owing to the ease with which temporary pressure may disorganize the delicate nerve apparatus of the internal ear the loss of function will be permanent. The statistics of aural hospitals show that hereditary syphilis is responsible for a very large proportion of the cases of deafness in young adults and that the cases when advanced are irremediable. In most cases, and perhaps in all well-marked ones, both ears are affected, and although as in the case of the eyes one may take precedence of the other, it is usually only by a very short time.

This form of deafness does not appear to afford any close parallel with that which occurs in acquired syphilis, since in the latter inflammation of the internal ear is usually one of the secondary symptoms and occurs simultaneously with iritis, etc. The subjects of acquired disease are no more liable to have their ears fail many years after the primary disease than they are to suffer from interstitial keratitis.

Syphilitic Lupus.

The almost complete absence of tertiary symptoms, such as we see them in the acquired disease, is very marked when we contrast the two forms of syphilis. The almost entire immunity of the subjects of inherited syphilis from the forms of chronic disease, so common in the acquired disease, which we recognize as serpiginous sores of syphilitic lupus* has already been adverted to. Although I have been carefully on the lookout for such and have many times in public challenged their production, I have seen but four or five cases in which such a diagnosis could have been even suggested. Of two of these I possess portraits. One of them is not well characterized, and of the other, which is so, the history is very instructive and disproves the diagnosis. A mother and daughter were under treatment at the same time for the late results of syphilis. The daughter

* I prefer to employ still the now old-fashioned term, "syphilitic lupus," since it appears to me to designate the conditions more concisely than any other. The diseases so named are almost exactly in appearance like lupus, but they are amenable to specific treatment. My theory is that they occur in tuberculous subjects who have become syphilitic, and imply a partnership of the two infections.

was a girl of eight or ten, and she had large serpiginous ulcerations on her back. It was assumed that the child had inherited the disease, but eventually the truth was ascertained that she had acquired it in infancy. Thus her case conformed to rule and proved only that the disease when acquired in very early life may be followed by the same results as when obtained in adult age. This case well illustrates one of the innumerable pitfalls which attend the investigator of the phenomena of syphilis and the wisdom of the rule which declines to accept as proven anything which is exceptional to the general tenor of evidence.

On this topic Dr. Bulkley, of New York, writes: "I have seen in a girl twenty-three years old, exhibiting characteristically ragged and notched teeth and with a well-marked history of hereditary syphilis, ulcerative gummatous disease on the arm which had always been regarded as lupus, but which yielded rapidly and perfectly to proper specific treatment." This apparently is the only case of the kind which Dr. Bulkley's wide experience has afforded him.

Phagedenic Ulceration.

There is, however, a form of phagedenic ulceration somewhat, perhaps, allied to lupus, which is not very infrequent in inherited syphilis. It is rapid and destructive in its course and has its parallels rather in certain rare forms of acute ulceration, occasionally seen in the acquired disease, than in chronic and almost lifelong serpiginous processes. It is, in fact, a phagedenic ulcer and not a lupus, and is not attended by any precedent infiltration or formation of tubercles. It may be asserted that at no period of life do the subjects of inherited taint exhibit any form of skin disease which can be called lupus.

These phagedenic forms of ulceration occur almost exclusively on the face or in the throat. Their subjects are usually children approaching adolescent age. The edges of their ulcers show the usual characters of a relatively slow form of phagedena, being ragged as if gnawed and undermined. The process is often sufficiently rapid to destroy the whole of the soft palate or the greater part of the nose in a few months. At a certain point, and usually probably as the result of treatment, the disease is arrested, and when this is effected sound healing occurs with, it may be, extensive disfigurement, but with no danger of relapse. I do not recollect ever to have treated the same patient for two separate attacks.

The local nature of the malady is proved by the absolute necessity

which exists for vigorous local treatment and by the good results which follow it.

Cases in which the larynx has been involved in syphilitic ulceration due to inherited taint have been recorded by Dr. Percy Kidd and others. In Dr. Kidd's cases, two in number, the laryngeal disease occurred at the ages respectively of thirteen and fourteen. In several cases tracheotomy has been found needful. One of these in which subsequently stenosis of the bronchi occurred was brought before the Pathological Society of London by Mr. R. W. Parker. The patient was a boy of fifteen at the time of his death from lung disease. He had nodes on his tibiæ.

A remarkable example of the phagedenic ulceration which sometimes occurs in inherited syphilis has been recorded by Messrs. Harris and Simpson, of Manchester. A boy of fourteen, in whom the soft palate had been destroyed some years before, had a similar process attack his tongue. It began in the middle of the organ, and spreading to its sides, finally destroyed nearly the whole of it. The boy himself showed no other indications of syphilis, but his brother, a year younger, had the characteristic marks. I long ago made the observation that in cases of phagedena it is exceptional to find the teeth notched. This case remarkably confirms my statement, but it remains exceedingly difficult to give even a conjectural explanation of the fact.

Phagedenic ulceration of the nose, face, or palate is rather rapidly destructive if not promptly treated and may occasion great disfigurement. Iodide of potassium internally and liberal and repeated cauterization of the sore with nitric acid are the remedies. Powdered iodoform or chinosol should be dusted over the sore. No pains should be spared to secure speedy arrest of the process, and when once it has been obtained healing will be rapid and there is little or no fear of relapse.

Psoriasis palmaris and *plantaris* and also all chronic affections of the *nails* are very rare in the subjects of inherited syphilis who have passed childhood. In infancy the nails not infrequently suffer, and I have seen one or two instances of chronic affections in later life, but they are exceedingly infrequent.

Affections of the Tongue.

Amongst the tertiary disorders very common as the results of acquired disease, and infinitely rare as those of inherited taint, are all affections of the tongue. We encounter neither gummata, chronic ulcerations, nor sclerosis, and it would appear that the patients may

smoke with impunity. I have seen and recorded one single case, in a subject of inherited syphilis, in which a well-defined muscular gumma occurred in the substance of the tongue and was rapidly made to vanish by iodides. The patient was a woman of thirty—one of two sisters both of whom I had myself many years before treated for keratitis and with whose infantile and parental history I was well acquainted. This is, however, the only example of gumma in the tongue from inherited syphilis which I have ever seen, and the examples of more vague affections, such as chronic ulcers or scleriasis, have been exceedingly few. This exemption in adolescent and adult life is perhaps the more remarkable when we remember that the condition known as the ring-worm tongue is not very uncommon in young children and that some good authorities have attributed it to syphilis. Amongst these was the late Dr. Parrot, of the Paris Hospital for Sick Children, who had abundant opportunities for observation and who held that it was always of specific origin.* From the evidence which I have collected I cannot share Parrot's opinion, but am inclined to think that the affection in its most typical forms may be met with quite independently of any syphilitic taint. Some of my cases have, however, been very perplexing, for I have twice seen the affection in children, one of whose parents had to my certain knowledge had syphilis, but who had themselves never shown the least indication of taint.

I have never once seen cancer of the tongue in a patient who had inherited syphilis, although I have seen hundreds of cases in those who had acquired it.

Affections of the Bones.

Periostitis.—An encrusting and ossifying form of chronic periostitis is not uncommon. It affects especially the tibiæ, but may occur in any long bone. It is seldom or never seen on the skull. When affecting the leg bones, it may produce great thickening and also increase of length simulating the results of ostitis deformans. It is attended whilst in progress by much aching in the affected bones, but not by severe nocturnal pain. It usually comes to an end after a year or two. In exceptional cases suppuration may occur, and large superficial portions of bone may exfoliate.

In the treatment of this affection iodide of potassium in full doses must be tried, and if it fails we must resort to mercury.

Atrophy of the Long Bones.—The chronic ostitis which leads to

* Good illustrations of this peculiar malady, the best of them copied from Parrot, are given in the second volume of my work on Clinical Surgery.

great thickening of the bone affected, the sabre-shaped tibia, etc., are fairly common, but that there may also result a condition of atrophy is rendered probable by the reports of a few cases. A skiagraph obtained by my son from a syphilitic boy who sustained a fracture of the bones of the forearm showed the radius extremely attenuated in the whole length of its shaft and somewhat shorter than the ulna. Its epiphyseal ends were not affected.

Diseases of the Joints and Spondylitis.—The occurrence of joint affections in congenital syphilis has been carefully studied by my son in his lectures delivered before the Royal College of Surgeons. An important case by Mr. Bowlby with a discussion thereon before the Medico-Chirurgical Society will be found reported in *The Lancet* for October, 1892. Dr. Paul Gueterbock, with whom I had at the time the pleasure of much communication, was one of the first in 1878 to draw attention to the subject. He thought joint disease common under these conditions, but with the exception of the transitory affections which occur in association with keratitis subsequent experience has not confirmed this view. A few cases of affection of the joints and bones of the spine (spondylitis) have also been recorded by Ridlon, of Chicago.

Certain curious malformations of joints have been observed. These more especially affect the elbow-joint and probably result from epiphyseal inflammation in infancy.

Affections of the Testes.

Gummata.—In connection with the rarity of gummata the non-liability of the subjects of inherited taint to syphilitic sarcocele excepting in very early periods of life may be mentioned. Gumma of the testis constitutes in the acquired disease one of the most common and definite forms and may occur at various periods after the primary affection. In the subjects of inherited syphilis it is met with now and then during the first few years of life, but never, I think, later on.

Wasting of the Testes.—Professor Fournier, to whom we are much indebted for many valuable observations in reference to inherited syphilis, has noted the occurrence of lesions of the testicle in a considerable number of cases. He describes two conditions as affording valuable evidence of the existence of a syphilitic taint—a sclerotic atrophy secondary to gumma and an arrest of development, the glands remaining like those of an infant. I have seen a few examples of gumma and a few of arrest, but have not encountered either condition with sufficient frequency to induce me to look for them as aids in diagnosis.

Fournier's opinion that a considerable proportion of those who have suffered from inherited disease remain undersized and deficient in sexual attributes is probably well founded. I have figured in the *Archives of Surgery* (Vol. V.) the uterus and appendages from a case of this kind, their size being not more than half of what is normal. As noted below, however, this rule of arrested sexual development is not without its exceptions.

Enlarged Spleen with Hæmoglobinuria.

A very marked example of this condition was repeatedly under my care in the London Hospital many years. The patient was a lad of seventeen who was the subject also of enlarged liver. Dr. Sanford Knaggs and Dr. C. O. Hawthorne have also recorded examples. It would appear to be very rare. It finds its parallels in certain examples of Raynaud's phenomena with hæmoglobinuria which occur in the subjects of acquired syphilis.

Arrest of Growth and Dwarfishness.

In certain rare cases an arrest of growth occurs as a consequence of inherited taint and the patient remains a dwarf. It may be conjectured that in these the pituitary body may have been the seat of disease. In most of these cases it would appear that there is arrest of sexual development also, but this is not invariable. I well recollect a woman who was a dwarf and absolutely deaf as the result of inherited taint, but who had married and was the mother of a fine son who grew to be much taller than herself.

Long Persistence of the Taint and Transmission.

Dr. C. O. Hawthorne has recorded with great care the history of a syphilitic family in which the eldest born was healthy in infancy, but at the age of twenty-three suffered from keratitis. She had characteristic teeth. The three following pregnancies resulted one in miscarriage and two in children who died of water on the brain. A fifth pregnancy produced a boy who at the age of eighteen had characteristic teeth and periostitis with enlarged spleen and liability to hæmoglobinuria. This youth was between six and seven years younger than his sister. From a sixth pregnancy a boy was born a year younger than the last who (up to the age of seventeen) remained in robust health and free from all evidences of taint. After this a still-born male child was produced. In this instance no parental history

of syphilis was forthcoming, and we may assume that the taint persisted in the mother's ovaries for at least seven years. The insuperable fallacy, however, remains that one or other parent may have received a second infection prior to the birth of their fifth child which suffered most.

A very interesting narrative respecting a syphilitic family is given by Dr. Routh, of Manchester, in the *Medical Chronicle*. The mother had never ailed anything whatever, and the father had shown no symptoms of syphilis since his marriage. After two still-births a child was born who showed symptoms of hereditary taint in infancy and was cured by mercury. At the age of nine she had an enormous spleen and a nodular liver with some enlargement of glands, but not one of the ordinary stigmata of syphilis. Specific remedies did nothing for her spleen or liver. The next child, two years younger, had infantile symptoms and was treated. At the age of seven she had characteristic teeth and rickets, but no other signs of syphilis. A third child suffered slightly in infancy, but was not treated, and at the age of two became during sleep hemiplegic in his right side. Two children born subsequently were quite healthy. The narrative well illustrates the irregularity which so often obtains in the transmission of syphilis, one child presenting one symptom and another another. The absolute freedom from symptoms of both parents notwithstanding the long persisting transmission is of interest. The final dying out of the taint, although no treatment had been adopted, is only what is usual.

Latent Syphilis.

It is a question of great speculative interest and of some practical importance whether in spite of our improved means of diagnosis any large number of cases in which syphilis has really been inherited escape recognition. The discovery of the meaning of notched teeth and interstitial keratitis has undoubtedly led to the recognition of this taint in a large group of cases in which previously it had not been suspected. Are there, however, still a considerable number in which neither the occurrences of infancy nor those of adolescence make the revelation? It must be freely admitted that this is possible, but the estimation of its extent is a matter of the greatest difficulty. If a child born with a syphilitic taint shows no symptoms in infancy, there is a certain amount of probability in the suggestion that it will show none in later life. The phenomena of tertiary disease are presumably for the most part recrudescences of what occurred in the secondary stage. This argument may not apply to such

affections as keratitis and the deafness of hereditary syphilis, since, as I have tried to show, these affections stand rather in the category of postponed secondary symptoms than of true tertiaries. They are bilateral, they subside spontaneously, and do not recur—three important features in which they differ most definitely from all truly tertiary phenomena. It is possible then that they might occur in those who had shown no symptoms in infancy, and as a matter of fact, they not infrequently do so. It is by no means unusual to encounter them in those who show no peculiarities of physiognomy and in whom the history of infantile symptoms is wanting. It is difficult to answer the question as to whether a child who wholly escapes infantile symptoms may yet show characteristic teeth. Such an event, though doubtless rare, may be held to be probable. The deformities of the teeth are not quite in the same category with the sunken nose, prominent forehead, and fissures at the angles of the mouth which make up the well-known physiognomy. These are all the results and direct evidences of infantile disease and would of necessity be absent if it had been omitted. It is not, however, proved that the deformations of the teeth are wholly of that nature, although it may be held probable that to some extent they are.

That infants in whose fluids the virus of syphilis is present in an active form may yet show no symptoms is abundantly proved. In all the cases in which syphilis has been communicated in vaccination the vaccinifer was in the judgment of the vaccinator in sound health. We may feel quite sure that in none of these were any of the more obvious indications of taint present. Not only were they absent, but it is expressly recorded in some instances that the infant exhibited all the signs of vigorous health.* The same lesson is conveyed, and in only a slightly less conclusive form, by the numerous instances in which the subjects of interstitial keratitis are stated by their parents to have been in excellent health through infancy and childhood. We may assume that the presence of the virus of syphilis does not necessarily arrest the growth of the child or produce affections of the skin, mucous membranes, or other parts. It may be remarked in passing that a similar statement is no doubt true of the acquired disease. Not a few probably pass through the primary and secondary stages of syphilis without its being recognized and whilst retaining apparently good health. In the case of inherited disease there are

* This was especially the case with the vaccinifer in one of the series of cases which I published in 1874. The vaccinifer had been selected at a station as a specially healthy child, and remained apparently such after the vaccination which conveyed syphilis to sixteen individuals. A small and almost doubtful condyloma at the anus was the only symptom discoverable after the most careful search.

concomitant facts which may help us to an opinion. There is the parental history, and very frequently we find in addition the existence of syphilis in the brothers and sisters of the patient. From one or other of these sources light may often be obtained and suspicions confirmed. The investigation of histories including a record of all members of the family becomes of much interest in this respect. In examining these it is by no means unusual to find that whilst one child was undoubtedly the subject of taint, brothers and sisters born under conditions apparently similar as regards risk have appeared to escape, or it may be that the escape of such has been only partial—that, for instance, a child who had no infantile symptoms whatever yet becomes the subject of interstitial keratitis at puberty. Such cases are not infrequent, and they might, were it not for the corroboration afforded by the family history, be held to invalidate the creed that such keratitis is in itself a proof of taint. If, however, intervening between two children who show symptoms there is one to whom nothing whatever happens, are we to assume non-inheritance or suppression? The question becomes perhaps still more cogent in the case of twins when one suffers and the other apparently escapes.

It may be that the more rapid metabolism of the tissues of the young favors the elimination of specific poisons and of whatever they may leave behind them. It would certainly appear to be the fact that the subjects of hereditary syphilis get both more quickly and more completely rid of it than is the case with those who have acquired it. If an infant has passed safely through the outbreak of secondaries, it is but seldom that anything occurs during several years to again reveal the taint. Subsequently we may have the keratitis and the internal otitis, but these very peculiar affections stand almost alone, and are unattended by any of the more ordinary phenomena of the tertiary stage, which are so unfortunately common after the acquired disease. Nor can this comparative immunity be attributed to greater efficiency of specific treatment, for of this infants and young children often receive but little—certainly as a rule much less than adults receive.

Inherited Syphilis as a Cause of Idiocy.

The influence of inherited syphilis as a cause of idiocy, or of mental failure, although unquestionable as a fact is probably very small in extent. Drs. Shuttleworth and Fletcher Beach, dealing with the inmates of idiot asylums, have arrived at the conclusion that not more than 1.17 per cent. are the subjects of inherited taint. Dr. Telford Smith has arrived at conclusions almost identical. Of five hundred and eighty idiots he found suspicious features in physiog-

nomy, etc., in eight, but only in three of these was the diagnosis supported by the parental history. It may be believed that the greater portion of these cases are examples of paralytic dementia developed during childhood and not of congenital defect in the brain. Dr. Shuttleworth has remarked, and I can fully confirm his observation, that in most of these cases there has been a period during which the child appeared to be in excellent health. Some good illustrative cases are recorded on page 218 of Vol. V. of the *Archives of Surgery*. The malady is perhaps the analogue of the general paralysis of the insane (*dementia paralytica*) met with in connection with acquired syphilis.*

The diligence of observers, earliest and foremost among whom I must mention Dr. Hughlings Jackson, has placed on record many and various forms of disease of the nervous system in the subjects of inherited taint. There is, however, good reason for maintaining that they are very infrequent, and that in the vast majority of cases these patients when past the period of infancy enjoy good health. At any rate there cannot be the slightest foundation for the suspicion that inherited taint threatens to be a cause of mental deterioration of the race.

Tabes Dorsalis.

Not only are the common tertiary maladies rare in the subjects of inherited syphilis, but the important class of what we may call aggressive degenerations, to which we attribute tabes dorsalis and general paralysis of the insane, are almost absolutely unknown in them.

Now tabes is a really common sequence of acquired syphilis in the male sex. If it be alleged that its non-occurrence in the cases which we are now considering is to be explained by their relative fewness, we certainly have reduced to a very minimum the facts upon which is based the fear that hereditary syphilis may become one of the causes of degeneration of the human race. It has never occurred to me in any single instance to identify the subject of this inheritance in a sufferer from tabes or general paralysis, and the number to be found in our lunatic asylums in connection with any type of mental disease is exceedingly small. On the other hand, I have had a large experience with those whom I have known to have suffered from inherited taint in childhood and who in later life have preserved excellent health.

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* Both Parrot and Henoch have recorded their incredulity as to syphilitic taint ever being the cause of brain disease during intrauterine life.

Transmission to the Third Generation.

This statement of fact as regards the almost absolute immunity in adult life of those who in infancy have suffered from inherited syphilis may fitly introduce the topic of the possibility of transmission to the third generation. It seems improbable in the highest degree that those who have long ceased themselves to be liable to any manifestations of syphilitic taint should still be capable of transmitting it. Further, and perhaps yet more conclusively, we may allege that as in the acquired disease the liability to transmit the disease to the offspring appears to cease with the period at which the risk of direct contagion ends, it is not likely that this liability should be retained by one who probably does not become a parent until twenty years after the contagious period has been passed. No one will suggest that the adult subjects of inherited taint are liable to convey the disease by contagion, and it is just as improbable that they can transmit it by inheritance. In order that either contagion or transmission should be possible we must suppose that the specific virus is still extant and all the facts with which we are acquainted converge to the belief that the duration of its life in the system is in almost all cases limited. Nor have any facts been placed on record which are worthy of much attention as supporting the belief referred to. One of the strongest of them is, I believe, a case recorded by myself. A married woman came under my observation for keratitis of an undoubted character. She had a baby which she said was healthy, but which, when brought to me, was found to be suffering from symptoms of inherited syphilis. It was, however, by no means certain that her husband had not himself had the disease. This same fallacy is present in all cases of supposed transmission to the third generation and is not least to be suspected when most vehemently denied.

An excellent critical summary of these cases is given by Dr. George Ogilvie in the *British Journal of Dermatology* for 1897. One of the cases which Ogilvie finds the strongest is recorded by Dr. Cæsar Beech. A woman, herself the subject of inherited syphilis, bore three children, the last of whom alone presented signs of syphilis, the second having lived two years in good health. Now this woman's first-born was illegitimate, and there was nothing in her character to induce a feeling of confidence as to the paternity of her last.

Those who are not fond of allowing isolated exceptions to become the basis of a general creed will surely in this matter do well to withhold their acquiescence until a much more critical judgment has been

displayed than is evinced in most of the records on this matter. It is better to believe that which the general tenor of evidence makes probable than to accept as proof little fragments of what may be claimed to be positive evidence, but which is really not out of reach of fallacy. If transmission to the third generation were possible, it ought to be fairly common, and we ought soon to be in a position to entertain no doubt about it.

Congenital Immunity.

It has probably been taken as granted by most that when a woman suffering from syphilis in the secondary stage bears a child which shows no signs of taint the escape of the latter is only apparent. We owe, however, to Behrend the definite statement that such a child may be suckled by its mother with impunity and will not contract the disease from her. This observation having been repeated by Profeta, has obtained the name of *Profeta's law* and has under that name been extended so as to include a general immunity as regards syphilis on the part of all offspring of syphilitic parentage. If it be strictly understood that such inherited immunity is acquired only by the offspring of parents who were at the time suffering from syphilis in an early and active form, it is very probably well founded. It is indeed Colles's law reversed and applied to the offspring instead of to the parent. It is not probable that cases especially fulfilling these conditions are numerous, although there are plenty of instances of children born during early periods of the maternal disease who remain apparently free. My own memory supplies but one example in which I actually witnessed the secondary stage in a pregnant woman and the child was born and remained healthy. In this instance I have watched the child from infancy to ten years of age, and not a single symptom has occurred. The possibility of keratitis, however, yet remains. The mother was, of course, actively treated with mercury during the latter part of her pregnancy.

There is nothing improbable in the supposition that as a rule a child shares any taint which its mother may possess, and the mother that of her child. Thus a child obviously diseased cannot infect a mother apparently healthy, and a mother obviously diseased cannot infect her child, although apparently healthy. In each instance the freedom from taint in the one is only apparent and not real. No doubt this is the general fact, and "Profeta's law" is confirmed by general experience, just as is that of Colles. To both exceptions may doubtless occur, and it must never be forgotten that in all cases the immunity conferred by a specific disease is only temporary. This

applies to vaccination and to smallpox itself. As to the duration of such immunity, we have no facts which would lead us to believe that it can be assigned with precision. It appears to depend largely upon the idiosyncrasy of the patient. A case is, I believe, well authenticated in which a woman took smallpox five times and died in the last attack. In some persons vaccination will "take" over and over again. With such facts before us, no wonder need be expressed that some persons are liable to reinfection of syphilis after a comparatively short time, although unquestionably, as a rule, a long period of immunity is conferred. That the so-called law of Profeta ought not to be extended so as to cover the alleged fact that whole nations have acquired some degree of immunity is obvious, since no one holds that under the worst conditions more than a very small proportion of children are born of parents in the stage during which alone transmission is possible.

Prevalence and Severity of Inherited Syphilis.

The estimate entertained by certain sections of the public as to the prevalence of inherited syphilis is, I feel sure, a very gross exaggeration, and the same is probably true, though to a lesser extent, of that which obtains in the profession. The diagnosis in all stages is often very difficult, and the simulations of syphilis, both in infantile and adolescent periods, are very numerous. My personal experience is with the patients brought to me in consultation as suffering from inherited taint, and only in quite a minority of these am I able to confirm the suspicion. The statement that syphilis is likely to become a cause of degeneracy of race is one from which I most utterly dissent. The disease is probably much less common than it was in the sixteenth century and is gradually becoming less so, and the extent to which its hereditary transmission influences the well-being of the community is exceedingly small. The fallacies to which allusion has just been made will suffice to explain the omission of any attempt to appeal to statistics. The construction of statistics on this subject is not possible. According to the Registrar General's reports for England the deaths from syphilis in children under one year old were, in 1878, 219 per 100,000 living; in 1883 the number rose to 235, but it has ever since been decreasing, and in 1897 was only 170. Dr. Birkbeck Nevens, who has made a careful attempt to estimate the prevalence of syphilis in children's hospitals, arrived at the figures of 14 in every 1,000 in 1875 and only 8 per 1,000 in 1895. To what extent the cheerful impressions which such statements convey are well founded it is impossible to say. Nor if shown to be trust-

worthy as facts would it be easy to give their correct explanation. The years under consideration have been years of prosperity, and it may have been that early marriage having been more easy of attainment, syphilis as a whole may have diminished, and the children of the poor may have been better cared for. On the other hand, it may easily have been the case that improved methods of treatment explain the whole and that the difference is in fatality and not in prevalence. In illustration, however, of the need for caution in accepting the facts, I may mention that according to some statistics supplied to me in 1887 by the late Sir George Buchanan the total number of deaths from syphilis of children under one year of age, which was in 1855 only 579, had risen in 1885 to 1,652. A deduction from this apparently large increase must, of course, be made for increase of population. It is very possible that all the remainder is to be attributed to changes in nomenclature.

Syphilis Acquired in Infancy.

It seems to be proved that the acquisition of syphilis by a young infant after birth may produce just the same results as its acquisition in utero or its sperm or germ inheritance. This is a very important step in our knowledge. The cases recorded in proof of it are two, and they come from different and distant observers. In one of these, Dr. Welander, of Stockholm, states of a boy who had acquired syphilis from his nurse when three months old that at thirteen years he had interstitial keratitis and nodes and that his teeth were characteristic. The second case was brought before the Paris Society of Dermatology by M. Eudlitz. The patient, now twenty-three years old, is small in stature, beardless, and with atrophied testicles. He has characteristic teeth and has been under Fournier's care for cerebral syphilis. The history is that he acquired syphilis at the age of two months from his mother, who had herself been infected by a nursling.

Treatment.

As regards the treatment of patients who are the subjects of inherited syphilis, it is obvious that different rules must be formulated for the different periods of the disease. A general consensus of the profession declares that the influence of mercury upon young infants suffering from active secondary symptoms is usually good. Some of the most noteworthy of our therapeutic triumphs are often obtained when mercury is judiciously employed for infants who are the sub-

jects of syphilitic cachexia. They fatten and thrive under it. The precise mode of administration does not matter much. Small doses of the perchloride in solution, of the hydrargyrum cum creta in powder, or of mercurial ointment by inunction are all convenient methods. It is a great point not to use the remedy too vigorously. Of the three methods perhaps inunction is the best as being the one least likely to cause diarrhœa. I do not think there is any doubt that the use of mercury in infancy is very injurious to the second set of teeth. Nor is this an unimportant consideration in cases in which the remedy may not seem to be absolutely necessary. If an infant known to have inherited syphilis displays no symptoms and is in good general health, it is better to abstain from treatment. By doing so it may be thought that we increase the risk of developments at a more advanced age, such as keratitis, etc. This, however, is a matter by no means certain, whereas the damage to the incisor and molar teeth is inevitable. Many infants pass through slight early symptoms of inherited syphilis unrecognized and without specifics, and it has yet to be proved that they encounter greater risks in the future than do those for whom mercury has been used. If, however, the child's health fails, then without doubt mercury should be cautiously but at the same time efficiently used.

If in infantile periods there be bone tenderness or periostitis, iodide of potassium should be given. It should, however, be avoided unless clearly indicated.

When a child the subject of inherited taint is threatened with ear symptoms both mercury and iodides should at once be prescribed in as full doses as can be borne. There is no time to be lost, and the delay of a week or two may easily result in permanent and complete deafness. From this, I believe, not a few patients are saved by prompt treatment.

A statement almost similar might perhaps be made as to keratitis when seen in its early stages. Here, however, the penalty of delay is less cogent, for in a majority of cases, however severe and threatening may have been the inflammation of the cornea for a time, reparation is possible and will in the majority of cases proceed almost to perfect restoration of sight. It is true that many cases of keratitis advance apparently unchecked by specifics. This fact should not, however, discourage us in their use, for in a large number they appear to be of great benefit. Probably it is in the early stages that they are most effectual in arresting the morbid processes. Both iodides and mercury should be given, and at the same time atropine should be put into the eyes. In some of the most severe cases attended by much pain and great intolerance of light I believe that

the old-fashioned seton in the temple (put well back in the hair) is a very valuable means of relief.

In the persisting form of ostitis which sometimes occurs in childhood and which leads to thickening of the bone, the iodide of potassium should be first tried, but if it does not succeed in relieving the pain it should be helped by mercury. As a rule mercury aggravates the conditions in bone syphilis in both the acquired and the hereditary forms, but there are exceptional cases in which it relieves. These are, I think, especially those in which the bone is indurated and enlarged and in which there is no tendency to softening. I have known cases of this kind in which iodides had been given for a long period without benefit, but in which mercury brought relief.

We know little or nothing as to the prophylactic influence of specific treatment in reference to inherited syphilis. It is one of the many important problems which are left to the industry of future observers to determine whether prolonged treatment in the early stages tends in any material degree to prevent the development of the lesions which are prone to follow after long intervals. The reply in the affirmative which most would be inclined to give in the instance of the acquired disease cannot with anything approaching to the same degree of confidence be offered in respect to those of the inherited. The facts regarding the two are very different. As a rule we are content in the latter to subdue symptoms as they arise, and we usually abstain from treatment if the patient is in good health and free from symptoms of the disease. I have given some reasons for holding that this is the best practice in the case of young infants whose teeth are not yet calcified, but it does not follow that we ought to extend the same caution to later periods when the teeth are no longer in danger. It may be that a long course of small doses of mercury given at the age of from seven to ten would prevent the risk of keratitis and some other maladies.

The phagedenic ulcerations which are sometimes seen in the throat, on the nose, or less frequently on other parts are to be treated by iodides and mercury internally and, what is yet more important, by the sedulous employment of iodoform, chinosol, or caustics externally. In not a few cases of this kind the repeated application of fuming nitric acid will be found the most efficient means of stopping the ulcerative action. The disfigurements produced by these affections are often very considerable, and prompt and even severe treatment is necessary.

LEPROSY.

BY

PRINCE A. MORROW,

NEW YORK.

LEPROSY.

Synonyms.—Lepra; Elephantiasis Græcorum; Leontiasis, Satyriasis; French, Lèpre; German, Aussatz; Norwegian, Spedalskhed; Spanish, Elefantiasis de los Griegos; Italian, Elefantiasis dei Greci, Lepra, Lebbre; Latin, Lepra vera, Elephantiasis; Hebrew, Zaraath (Tsaraath); Sanscrit, Kushtha; Egyptian, Uchetu.

Definition.—Leprosy (from Greek, λέπρα) is a chronic infectious disease caused by the bacillus lepræ, characterized by erythematous and pigmentary changes in the skin and the production of tubercular nodules containing bacilli in the cutaneous tissues and mucous membranes, and by irritative and degenerative changes in the nerves, with implication of the lymphatic ganglia and internal viscera and the supervention of a profound cachexia which leads to a fatal termination.

Types of Leprosy.

The bacilli of leprosy, like the germs of other infectious diseases, when they have gained access to the organism, affect particular structures and spread from one organ to another along certain definite tracts, producing changes in the tissues which are characteristic and peculiar to the morbid process. These changes consist of diffuse or circumscribed infiltrations, and the clinical picture varies according to the localization of the lesions in the integument or in the nerves.

Two principal forms of leprosy are recognized. When there is a determination of the morbid process towards the cutaneous and mucous membranes in the shape of macules and nodules, it is termed *tubercular* or *tegumentary;* when it is centred upon the peripheral nerves, it is termed *anæsthetic, trophoneurotic,* or *nerve leprosy.* These two forms, although etiologically identical, exhibit marked differences in their objective characters, mode of evolution, and duration.

In tubercular leprosy the predominating lesions are nodular infiltrations, termed tubercles or lepromata, in the skin, mucous membranes, and other organs; the course of this form is more rapid, and the average duration of life is from five to fifteen years.

Anæsthetic leprosy is characterized by degenerative changes in

the nerves, anæsthesia, atrophy, and mutilation of the extremities; its course is slower, and the duration of life may be prolonged to fifteen or twenty years or longer.

As marks of differentiation it may be said that the development of tubercles constitutes the distinctive sign of the tubercular form, while insensibility and atrophy are the distinguishing features of nerve leprosy. While both forms almost invariably proceed to a fatal termination, both are susceptible of spontaneous cure—the anæsthetic form rarely and the tubercular form still more exceptionally.

The division of leprosy into two principal forms, according to the most prominent symptoms exhibited by each, was recognized by the early writers, and this classification is now practically universal. Certain writers have attempted to differentiate still further the manifestations of the disease by the employment of terms indicating a single symptom. Thus Kaposi and others describe a *macular form*. This cannot, however, be recognized as constituting a distinct form or type of leprosy. Macules simply represent a phase in the evolution of the malady common to both the tubercular and anæsthetic forms and do not exist independently, but are always associated sooner or later with tubercular or nerve manifestations.

That the above division of leprosy into two forms is to a certain extent arbitrary is evident from the fact that the typical features of both forms may coexist in the same individual, thus establishing their pathological unity. In a certain proportion of cases there is a combination of both tegumentary and nerve lesions, constituting what is termed the *mixed or complete type of leprosy*.

ETIOLOGY.

At the present time there is a general consensus of opinion among medical men that the vast array of functional disorders and organic changes met with in leprosy are caused by the introduction into the human body of a specific microorganism, the bacillus lepræ. The fact that this organism is invariably found in the body of lepers, and nowhere else, would seem to establish the relation of cause and effect between the presence of the bacilli and the production of the symptoms peculiar to the disease. It must be admitted, however, that the chain of evidence which connects the bacillus with the causation of leprosy is not so complete as in the case of certain other parasitic diseases, as for example tuberculosis and anthrax.

The rigorous conditions demanded by the modern scientific mind before we are authorized to affirm that the disease is of parasitic origin, produced by the introduction into the organism of a patho-

genic microbe, have not been complied with. These necessary conditions are:

1. That the specific microbe should be found in the diseased tissues.

2. That the microbe should be capable of being cultivated outside the human body.

3. That when the product of pure cultures is inoculated into the same species from which it was derived, it should produce the identical disease.

Since the bacillus has not been successfully cultivated or inoculated into animals, the scientific proof of its pathological rôle has not been demonstrated. Nevertheless, it is generally conceded that the theory of its pathogenic action is based upon sufficient histological and clinical evidence. This evidence has been formulated by Neisser as follows:

The constant presence of the bacillus in all cases which exhibit undoubted clinical evidence of leprosy; its localization in the diseased foci of the organism, so that every symptom of leprosy may be certainly referred to the bacillary focus existing *in situ* or at a distance; the correlation which exists between the cellular alterations within the cells and the bacilli; the fact that these bacilli present characters absolutely specific, and that leprosy possesses all the attributes and particularly the mode of propagation of bacillary diseases peculiar to the human race and transmitted from man to man. All these considerations admit of no doubt that the bacillus of Hansen is the unique and necessary pathogenic agent of leprosy.

The etiological views of writers on leprosy before the discovery of Hansen's bacillus have now only an historical interest. How various, diverse, and even contradictory these views were is apparent from the fact that at one time the origin of leprosy was attributed to divine wrath as a punishment for sin, at another time to divine favor, securing for the sufferers religious honors.

Viewed from the standpoint of our more advanced knowledge, we look upon these various theories of the origin of leprosy as only the speculations of human ignorance, and yet many of the theories which had been advanced are not only interesting, but also extremely valuable, as they indicate clearly the conditions under which leprosy ordinarily occurs.

The causes of leprosy have been variously ascribed to malaria, dampness and humidity, uncleanly habits, filth and overcrowding, sudden changes of temperature, etc. Dr. Tilbury Fox, writing in 1868, says the cause of leprosy is probably a mixed one. It is a combination especially of bad hygiene exhibited in damp dwellings, putrid and innutritious food, and a malarial climate. While the pathogenic

agent of leprosy escaped detection, there is no doubt that the causes alleged by these observers favor the propagation of the disease and to-day are recognized as powerful predisposing factors.

The Bacillus Lepræ.

The bacillus of leprosy, discovered by Hansen in 1874, is, as above intimated, now generally regarded as the essential cause of leprosy. In tubercular leprosy it is present in enormous numbers; in lepra

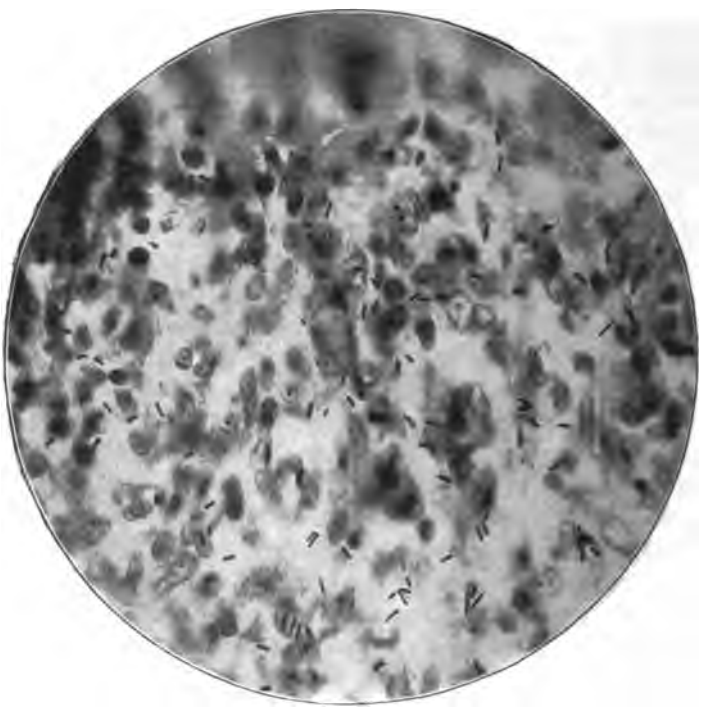

FIG. 1.—Bacilli Lepræ. (From a photograph by Dr. J. A. Fordyce.)

nervosa it is normally present in relatively small numbers. It has been claimed by Kaposi, Petrini, and others that it may be absent even in well-marked cases of tubercular leprosy. This paradox is explained in various ways. It is a known fact that under certain undetermined conditions the parasite stains very poorly and decolorizes rapidly, so that the technique may still be regarded as faulty. The failure of bacteriological researches to demonstrate the presence of bacilli in two cases of tubercular leprosy instanced by Kaposi cannot be considered proof that the organisms were absent, but rather that the methods employed were defective. On the other hand, the absence

of the parasite in lepra nervosa is regarded as evidence of spontaneous cure; at least of that particular attack.

Morphological Characters.—The bacillus lepræ is believed to belong to the Streptothrix family. It is a near congener of the bacillus tuberculosis, and a transition between the two is found in the bacillus of fowl tuberculosis. The members of this group are also believed to be allied to the actinomycetes, which are also pathological.

The parasite is slender and rod-like, in length from one-half to three-fourths of the diameter of a human red blood corpuscle, and in breadth about one-fifth of the length. The ends are usually pointed, but in certain cases are clubbed, and then resemble the Klebs-Löffler bacillus. Dichotomous division has occasionally been noted. Most authorities believe that the bacillus is spore-producing and also encapsulated. The tendency to form colonies is a characteristic of this parasite. Young bacilli are homogeneous, while the older are granular.

Analogies with Koch's Bacillus.—The points of agreement and difference between the bacilli of leprosy and those of tuberculosis are of more than passing interest. They show similar staining qualities, although the lepra bacilli stain with more facility, and both occasionally exhibit clubbing of the ends and dichotomy. The lepra bacilli are more uniform in size and rectilinear. They may be distinguished by differential stains, by their greater number, and by their tendency to form colonies.

The most striking point of affinity, however, lies in the similarity of their toxins. As the bacillus lepræ cannot be cultivated, we know of the leprous toxins only from their clinical results; but the similarity is shown by the fact that lepers react both locally and generally to tuberculin—a fact of great practical significance as holding out a plan for the rational treatment of the disease—a plan which, according to Babes, leads to at least temporary improvement when vigorously carried out over long periods.

None of the microorganisms cultivated from leprous tissues corresponds to Hansen's bacillus, although one of them, the so-called diphtheroid bacillus, much resembles it.

Methods of Examining for the Bacillus Leprœ.

In the Serum.—The best method is to clamp the nodule with a pair of forceps or a specially devised instrument for clamping and squeezing the nodule. After the nodule becomes anæmic from pressure it should be freely incised at the apex, when a small quantity of serum will escape. The clear fluid which exudes is to be placed upon a clean

cover glass, and if this is brought in contact with a second cover glass a thin film of exudation will spread evenly between the two, when they are to be carefully separated. The cover glasses are now passed through the flame of a spirit lamp, which fixes the film and assists in the process of staining.

The preparation is now to be stained in an aqueous solution of fuchsin, or better, a three-per-cent. solution of carbolic acid should be added to the fuchsin, which assists the staining-process. If now the specimen be decolorized in a thirty-per-cent. solution of nitric acid and counterstained with a methylene-blue solution, washed in water, dried, and mounted in xylol-Canada balsam, it will show the bacilli single and in clusters stained red, while the nuclei and ground substance are stained blue.

In the Tissues.—After the section is properly cut with a microtome it should be placed in a fuchsin-carbol solution for some hours. It should be removed carefully and dipped in a thirty-per-cent. solution of hydrochloric or nitric acid. This will decolorize everything except the bacilli. If the section is now stained with methylene blue, the red-stained bacilli will appear under the microscope as pink rods upon a blue ground.

Alvarez, of Honolulu, has proposed a rapid method of making a positive diagnosis in doubtful cases. After the removal of a bit of skin or other tissue to be examined it is washed in a normal salt solution and thoroughly triturated in a small mortar until a homogeneous solution results. The skin or other tissue may be boiled, or digestive ferments may be added, before it is submitted to the process of trituration. When the trituration is completed, a small quantity may be transferred to a cover-glass, and the specimen is then fixed, stained, decolorized, and counterstained in the manner described above. If there are but few bacilli present, the triturated mass may be submitted to a centrifugal machine or placed in a conical glass, and the sediment examined in twenty-four or forty-eight hours.

Alvarez claims that by this method we can spread upon the cover-glass films thinner than any section that can be made with a microtome, and by using the centrifugal machine we can gather bacilli in a small place, where they are easier to find than in a section. Moreover, a diagnosis can be made in a few minutes instead of waiting for the tissues to harden.

Culture Experiments.

Experiments in the artificial cultivation of lepra bacilli in various culture mediums have uniformly failed. The authenticity of cultures claimed to be successful by numerous investigators have all been con-

tested, since in no instance has the pathogenic nature of these cultivations been established by inoculation experiments.

Possibly an explanation of the uniform failure of all culture experiments is that due regard has not been paid to the element of time, which is so essential a condition of the germinative capacity of the lepra bacillus, and results may have been looked for too early.

Quite recently Carrasquilla, known as the originator of the serum therapy of leprosy, claims to have made successful cultures of the bacillus lepræ. His method of procedure and results are described in a communication to the National Academy of Medicine of Bogotá, February, 1899. He collects the serum by means of a specially devised clamp or forceps applied to the tubercles, macules, or infiltrations. The clear fluid collected is first examined under the microscope to be sure that it contains Hansen's bacillus. Tubes of gelatinized serum are then sown with a drop of the clear fluid on a sterilized platinum wire and placed in a Roux condenser at a temperature of 37° C.

At the end of twenty-four hours he saw the development of the first culture. Spots or macules had appeared all around the points sown with the platinum wire, with rounded, irregular contours, some yellow, others white with a certain refraction. Four days later he examined under the microscope the colonies of the first tubes sown and was able to demonstrate the presence of the bacilli, even without coloration. Submitted to the ordinary coloring methods, all the characteristics of Hansen's bacillus were displayed, while no other microbe appeared in the preparation, showing that it was a pure culture. Taking this first culture, he sowed other tubes of gelatinized serum, and these produced exactly the same development as the first, which were sown directly from the leprous exudation. Later he used as a culture fluid the bouillon of beef with identical results. One set of tubes was sown with the culture of preceding tubes, and the same series of phenomena was always produced under identical conditions. A month later, in examining the cultures, he was surprised to see the bacilli in movement, and in examining cultures there was always observed a mobility of the bacilli after a certain stage of their development. He was also enabled to identify different phases in the evolution of the microbes as shown by differences in their morphological characters and movements.

Carrasquilla further claims that, when injected into horses, the filtered liquid of the cultures produced precisely the same effect, although the reaction was more intense, as the serum taken directly from lepers. Furthermore, the serum of the horses which had received inoculations of the liquid from the cultures produced in patients the

same reactions and the same modifications in the manifestations of the disease, only perhaps more pronounced, as the serum from horses which had been inoculated with the serum of lepers.

Carrasquilla does not believe that the immunity of animals to leprosy is so absolute as has been maintained, and since experiments in inoculating human beings are not permissible, his further experiments are to be conducted with a view of reproducing the disease in animals by means of his cultures.

Until this final proof of the pathogenic action of the cultures is furnished Carrasquilla's claims must be received with the same scepticism as has been accorded by the profession to those of Bordoni-Uffreduzzi of Turin, Spronck of Utrecht, Byron of New York, and others, who have announced successful results in cultivating the lepra bacillus.

Distribution of the Bacilli.

Leprosy, according to Cornil, is the perfected type of bacterial disease. By the extreme abundance of bacilli infiltrated everywhere in the pathological products of leprosy, by their persistence at all periods, this disease gives us the most characteristic histological demonstration of the rôle of the bacillus. No other disease is so rich in bacilli. All leprous products contain colossal quantities of bacilli.

Like all specific microbes, the lepra bacillus has an elective affinity or predilection for certain tissues and fluids of the body. The bacilli are present in all forms and stages of tubercular leprosy; they are found in both the diffuse and nodular infiltrations of the skin and mucous membranes, in the connective tissue of the peripheral nerves, in the spinal cord (the anterior horns) and in the spinal ganglia, in the cornea, the cartilages, and the liver, spleen, and kidneys, sparingly in the spermatic tubes and testicles, also in the ovary and the female breasts. They are found abundantly in the lymphatic glands and spaces, in the sebaceous glands, and in the hair and sebaceous follicles of the body, but not of the scalp. They are not found in the blood, except in the last stages of the disease. It is claimed that they exist in the blood during the febrile or congestive attacks, but this has not been determined. The blood would seem to serve as an agent of transport for the dissemination of the bacilli through the economy. The bacilli exist in a state of permanence in the lymph, and this fluid is regarded as the natural culture fluid of the microbes.

Their presence in the *physiological secretions*, the tears, saliva, milk, and semen, though formerly denied, is now attested by Babes; they have never been found in the urine, nor in the menstrual fluid. It is probable that the physiological secretions, unless pathologically

altered by the presence of leprous deposits in the secretory structures of the organs, do not contain leprous microorganisms. The bacilli are, however, also found upon the skin and in organs which are to all appearances perfectly healthy.

The *pathological secretions* from the surface of ulcerating lesions of the integuments, of those of the mucous membranes of the nose, mouth, and throat, the large intestine, and the rectum contain large numbers of the bacilli, which are discharged through the nasal mucus, the saliva, and dysenteroid excrement in vast quantity.

It is to be observed that individual cases may present the greatest variations in respect to the lesions and secretions which contain bacilli. Thus Weber found that bacilli were in one case present in skin scrapings, lanugo hairs, blood from nodules, serum from vesicles, semen, etc., and entirely absent in the saliva, nasal mucus, scalp hairs, and in blood not taken from nodules.

The special reactions between the bacillus and individual tissues are best treated of under particular headings. With regard to the migration of the parasite within the body and the problem of its preference for individual tissues, we are still in great obscurity.

Elimination of the Bacilli.

The bacilli leave the body by means of every natural secretion or excretion, with the possible exception of the urine—in saliva, nasal mucus, conjunctival secretion, vaginal, urethral, and uterine discharges, semen, milk, fæces, secretion of leprous ulcers, and the free surface of the skin. They have not been found in the menstrual blood (Babes).

The nodules and diffused infiltrations of the skin and of the mucosa of the nose, mouth, and throat, the large intestine, and the rectum contain immense numbers of bacilli which are set free on the breaking down of these tissues. Once freed from their nidus, their dissemination is a matter of chance.

Schäffer claims that lepers throw off fewer bacilli from the skin than from the buccal and nasal mucosa in coughing and sneezing. He was able to collect lepra bacilli on clean slides placed on tables and the floor near to patients whom he had caused to read aloud. Lepers who had been reading aloud only ten minutes projected from forty to one hundred and eighty-five thousand bacilli.

The Bacilli Outside the Body.

Bacilli have been found in the habitations of lepers, articles of furniture, and objects surrounding the leper. They have also been found sparingly in the dust and dirt of rooms where lepers have lived, in the soil habitually trodden by lepers' feet, and in the earth where lepers have been buried.

From the fact that the leper discharges from his skin and nasal and buccal mucous membranes, and with his breath in talking, coughing, sneezing, etc., myriads of bacilli, and that these bacilli must of necessity come in contact with a large entourage of healthy people, none of whom may be contaminated, it is evident that these bacteria are either endowed with a very feeble contagious activity, or that they are dead or cadaveric when discharged. This cadaverization of the bacillus explains, according to Besnier, the negative results of cultures and inoculations and enables us to understand why it is that leprosy is wiped out when the leper dies, offering a new and fundamental distinction from Koch's bacillus which retains its vitality and virulence through an incredible length of time and under various conditions. The question whether the bacilli found outside the body are living or dead is still *sub judice*, and cannot be decided either affirmatively or negatively until we are able to show some comprehensible difference between living and dead bacilli by culture or inoculation.

Arning states that the bacilli seem to multiply in the bodies of dead lepers months after they have been buried. He has also observed that fragments of lepromata placed in water for several months became surrounded with myriads of bacilli, very evidently multiplied, and which proves to him that they are living.

Babes also concludes from certain characters of the bacilli, the globi and the appearances of sporulation, that some of them, at least, are living.

Transmission of the Bacilli.

As the bacillus lepræ has not been cultivated we have no certain means of determining to what extent the bacilli which infest the numerous secretions and discharges are lifeless, and for the same reason we have no positive evidence as to how the disease is spread.

Since the bacilli are present in the semen at an early period of the disease, although a condition of azoospermia soon supervenes, and the milk of women with tubercular leprosy also contains the parasite, Babes believes we are warranted in the assumption that bacilli may pass between two individuals in the processes of generation and lac-

tation. This would not, however, necessarily indicate that the disease was inherited. The ovary also contains bacilli, but much less frequently and to a less extent than the testicle.

Of other modes of transmission, direct and indirect, Babes thinks that the aerial route from the germ-impregnated dust to the pores of the face, especially when the pores are large and the subject uncleanly, has the most to recommend it. The reasoning to establish this belief is not *a priori*, but is based upon the peculiar small perifollicular foci of infiltration which are so characteristic of tubercular leprosy of the skin. Under the microscope this phenomenon is suggestive of the possibility of the penetration of the bacilli through the follicular wall from without. The converse, namely, the penetration of the follicular wall from within outwards in advanced cases of tubercular leprosy, is well authenticated, and by this means the bacilli, which appear to be unable to make their way through the epidermis, succeed in reaching the free surface of the skin when the latter is still unbroken.

Babes himself warns against too hastily adopting this view. We only know that the hair follicle is a predilection locality in leprosy, and under these circumstances the parasite may be able to reach it, no matter how it has entered the body.

With regard to other possible modes of transmission, we have no guide but the analogy of other diseases. In addition to the lodging of germ-laden dust in large pores and abrasions, the bacilli may find ports of entry through the mucous membranes of the nose, tonsils, conjunctiva, the deeper air and food passages, and perhaps the genitals, since primary lepromata are occasionally seen in the latter locality. When we come to lepra nervosa, the question of transmission becomes even more obscure.

In connection with this whole question it is well to remember that thus far there is absolutely no certain evidence of the disease being conveyed by inoculation.

Resistance of the Bacilli.

The resistance of the bacilli to disintegration and decay is most remarkable. Thousands of bacilli have been found in a small fragment of a leprous nodule which had become dried in an envelope of paper, where it had been forgotten for ten years. Bacilli may remain almost indefinitely in tissues where they are developed, showing no tendency to be eliminated or destroyed ultimately (Cornil and Babes). When introduced experimentally, bacilli have been found in fragments of nodules which had been inserted under the skin of animals one to two years previously.

Wesener's experiments would go to show that, unlike the bacilli of tuberculosis, lepra bacilli, if introduced in the living tissues, remain unabsorbed and susceptible of being impregnated by coloring matter for an indefinite length of time. He found the results to be identically the same, whether he introduced pieces containing bacilli which had sojourned in alcohol for two years or fresh pieces. In both cases the only manifest reaction was of a phlogistic nature, of a purely local character, and similar to that which would have followed the introduction of any inanimate matter, such as charcoal or cinnabar. The bacilli become incorporated with the cellular elements, and their form persists intact.

Variations in the Bacilli.

Variations in Staining Qualities.—In a communication to the Berlin Leprosy Congress, 1897, on "The Bacillus of Leprosy in the Human System at Different Periods of its Growth," Lawrence Herman has demonstrated that these variations are especially manifest in relation to the staining reactions of the bacilli. He found in a mass of bacilli which he extracted from tubercles and in sections that the bacilli did not all color in the same manner. The bacilli from recent nodules retained less carbol-fuchsin and took on a secondary coloration of methylene blue. In preparations from older nodules there are seen in the blue-stained masses, now and then, bacilli which have retained the fuchsin and are stained red. He has encountered: 1. Red-stained bacilli which have remained well stained deep red; 2. pale red-stained bacilli which have become decolorized to a greater or less extent; 3. bacilli which have lost their fuchsin and become stained more or less blue.

Herman concludes from his investigations that the bacilli which are easily decolorized and have by contrast taken the methylene-blue stain are the more recent and active bacilli, while those which have retained the red stain and are more resistant to the decolorizing effect of nitric acid represent the older, possibly more stationary forms.

Further researches are necessary before it can be determined whether the tinctorial differences between bacilli of different ages indicate a modification in their infective virulence.

Variations in Virulence.—*A priori* it might be assumed that specific bacilli possess the same character and degree of virulence irrespective of the source from which they are derived. Experiment has shown, however, that cultures of tubercle bacilli from bone tuberculosis are more highly virulent than cultures of sputum bacilli, and it is also claimed that different varieties of human tuberculosis exhibit marked differences in their respective virulence.

Since successful cultures of the lepra bacilli have never been made, the determination of their comparative virulence must be based upon clinical evidence alone. Observation would seem to show conclusively that differences in the virulence of leprous germs are manifest not only in respect to their contagious activity, but also in respect to the intensity and severity of their pathogenic action when introduced into the body. It is well known that leprosy is feebly contagious in certain countries and ultracontagious in others, while the virulence of the morbid process in the tubercular form contrasts with its comparative benignity in the anæsthetic form.

The causes of the great diversity in the objective characters and course of the two principal forms of leprosy, the rapid multiplication of the bacilli and their predilection for the cutaneous tissues in the one form, their comparative fewness and preference for the nerve structures in the other, has been variously interpreted. It was a subject of inquiry by the recent Berlin Leprosy Congress, and by certain leprologists the difference was attributed to the variable virulence of the bacilli.

Hansen considers it a begging of the question to invoke a variable virulence of the bacillus or a predisposition and a relative immunity of the soil; he thinks that climate influences the form.

Blaschko thinks there is no essential difference between the two forms, but only a difference in the quantity of the bacilli.

Arning, on the contrary, regards the difference as fundamental and believes that the bacilli have a different action in the two forms.

According to Neisser, it is not a simple difference in the quantity of the bacilli, but a qualitative difference in the morbid process, besides a different localization, it being in the cutaneous form proliferative and in the nerve form atrophic and retractive.

Impey thinks that there are either two very similar but not identical bacilli in leprosy, or that in pure nerve leprosy the poison secreted by the bacilli acts in a more powerful manner upon the nerves, because the nervous system of the patient is peculiarly susceptible to the effects of the ptomain.

In the writer's opinion the explanation of the difference in the two forms must be sought for, not in a difference in the virulence of the germs, but in the character of the soil. The type or form of the morbid process is determined by the idiosyncrasy of the individual or by some pathological predisposition which in the one case renders the skin, in the other the nerves, more susceptible to the pathogenic action of the bacilli. As regards the infective virulence of the bacilli, it is claimed that the tubercular form is highly contagious, while the other is comparatively innocuous. This may result not from a differ-

ence in the virulence of the germs, but simply from the accident of their localization, which in the one form permits of their abundant and ready discharge, while in the other they are chiefly confined in the nerve structures.

At the same time there can be but little doubt that the infective virulence of leprous germs is modified by climate and conditions of environment which render the system sterile or antagonistic to their development.

Inoculation in Man.

Before the bacillary origin of leprosy was demonstrated and during the period when the theory of the non-contagiousness of leprosy was in the ascendency, numerous attempts were made to inoculate human beings. At the present day it would be difficult to find any one who would dare attempt to inoculate leprosy.

In 1844 Daniellsen, who was a firm believer in the non-contagiousness of leprosy, first inoculated himself with portions of a tubercle from a leprous patient. He repeated this experiment on himself later in the same year without other result than the production of a septic lymphangitis. Still later, he inoculated two helpers and one nurse in St. George's Hospital in Bergen, all with negative results. In 1846 he inserted a small leprous nodule under the skin of his left forearm and the wound was sutured. The sutures cut through, and after a few days an ulcer formed which healed in a few weeks.

In 1856 Daniellsen, his assistant, Loberg, a farmer, two waiters, and a servant at Lungegaard's Hospital were inoculated with portions of tubercles, blood, and the pleural exudation from a leper. In 1857 several syphilitic and favus patients were inoculated, and in 1858 Daniellsen and a waiter were again inoculated, with negative results. The inoculations were ordinarily made in the arm, and when the leprous products were inserted the wound was sutured and covered with plaster. There were ordinarily redness and swelling over the sutures and after about fourteen days the individuals were all right.

Altogether Daniellsen inoculated twenty healthy individuals with the blood of lepers, portions of tubercles, and blood collected from the surfaces of the tubercles. There were observed a few cases of lymphangitis, but in none of the twenty cases did he produce a condition resembling leprosy. Some of these patients were kept under observation many years, but all remained perfectly healthy. The negative results of these experiments contributed largely to confirm the opinion that leprosy was neither contagious nor inoculable.

Profeta, between 1868 and 1875, inoculated himself, Cagnina, six men, and two women, all with their free consent, but the results

were negative. Bargilli of Mytelene made two unsuccessful inoculations.

Hansen inoculated the products of tubercular leprosy in persons already suffering from anæsthetic leprosy without result. Both Hansen and Beaven Rake also found that the local lesions of leprosy were not produced when the diseased tissues from a leper were inserted in a healthy part of the same person, which would seem to indicate that the bacillus does not grow in healthy tissues of the leper, but only in a part made suitable for its reception and growth by a process of preparation not yet determined.

In addition to these experimental inoculations, which were undertaken with a definite scientific object in view, may be added accidental inoculations, in cases of physicians or nurses who have pricked or wounded themselves in dressing the open sores of lepers and in performing operations or autopsies. In none of these cases has leprosy developed.

Reference may also be made to cases in which leprosy is said to have been contracted by thrusting a needle or knife which had previously been passed into the tissues of a leper into the tissues of healthy individuals in a spirit of bravado, as in Hildebrand's case, and to Blanc's case of leprosy following a razor cut in an English nurse, etc. These cases are open to the possibility of doubt as to whether the disease was inoculated in the manner alleged, as the patients were in more or less constant intercourse with lepers, affording abundant opportunities for infection in other ways.

The only experiment claimed to be successful in inoculating leprosy in man was that of the convict Keanu of Hawaii, who was inoculated by Arning in 1884 with pus laden with bacilli, and, in addition, a portion of a tubercular nodule was inserted subcutaneously. This man developed leprosy from which he has since died. In 1889, on a visit to the leper settlement of Molakai where Keanu had been sent, I excised a small cutaneous nodule from his arm with a portion of the overlying skin. Bacilli were found abundantly in numerous specimens of this section. The scientific value of Arning's experiment has been nullified by the fact that Keanu came of a leprous family, and it is not at all improbable that he had the seeds of the disease in his system previous to the experimental inoculation.

Inoculation in Animals.

All attempts to inoculate animals with the products of leprosy have been uniformly unsuccessful. Almost every species of animal life has been subject to experimental inoculations. Hansen endeav-

ored to inoculate cats, rabbits, and monkeys. Köbner inoculated monkeys, frogs, and various species of fish. Hillairet and Gaucher inoculated swine, but without results. Neisser, in inoculating dogs and rabbits, and Damsch, in inoculating mice and cats, have produced local manifestations of the disease in the tissues surrounding the nodule of inoculation.

Leloir inoculated five rabbits with pieces of tubercular nodules, introduced under the skin and into the peritoneal cavity. In one case, after six months bacilli were found in the nodules, but none in the surrounding tissues. In another case he found bacilli in the tissues, but regarded them as bacilli coming from the nodule of inoculation, and not as new bacilli which had been produced by the process of growth and multiplication.

Beaven Rake inoculated cats, introducing the leprous material under the skin, in the peritoneal cavity, and in the anterior chamber of the eye. These he kept under observation for four or five years, but without finding any local growth or general dissemination of the bacilli. Hansen inoculated animals with what he presumed to be pure cultures of the bacilli with negative results. Melcher and Ortmann reported that they succeeded in inoculating a rabbit by the insertion of a portion of a leprous tubercle in the anterior chamber of the eye. The animal remained apparently healthy, but suddenly died several months later. The lungs, heart, and pericardium were found to be the seat of an apparently fresh tubercular eruption. In the affected parts large round and oval cells were found containing bacilli which the authors regard as lepra bacilli and not tubercle bacilli. Later they reported that they had succeeded in inoculating two rabbits which died four months after inoculation. The whole of the viscera was the seat of a nodular eruption which they regarded as leprous. The similarity of the tuberccle and lepra bacilli and the difficulty of differentiating the nodules of tuberculosis from the nodules of leprosy must be considered in appreciating the value of these experiments. Feeding with leprous tissue has also failed to give results.

Dr. J. F. Dixon, medical superintendent of Robben Island Cape of Good Hope, has contributed some curious facts illustrating the immunity of animals to leprous infection. He says (*Journal Leprosy Investigating Committee*) "the domesticated animals of Robben Island have furnished additional evidence on the question under consideration for many years past and may be almost spoken of as having conducted an unsolicited series of experiments on their own persons which are of grave significance in this inquiry.

"Until quite recently the cows, and more especially the calves, were in the habit of consuming large quantities of poultice recently

taken from leprous ulcers and thrown out into the compound, and rags and cloths that had been used in binding up leprous sores. The poultry also used to eat discarded food and refuse thrown from the leper wards.

"The water in which the soiled and filthy clothes and rags of the lepers had been washed (in cold water only) was allowed to run down an open gutter of considerable length and was drunk regularly by the cows, calves, and poultry of all kinds.

"This had been going on for many years, and all the time the flesh of the animals and poultry, the hens' eggs, and the milk of the cows had been freely and constantly used by all sections of the inhabitants, who nevertheless remained healthy. The general health of the cattle and poultry on the island is excellent, and the conclusion seems inevitable that leprosy is not transferable through the medium of the lower animals."

Sources of Infection.

Recognizing Hansen's bacillus as the active efficient cause of leprosy, it may be assumed that all of the tissues of the body of the leper containing this organism constitute possible sources of infection; the conditions of infection being that the bacilli should be discharged from the body of the leper, brought in contact with and be capable of penetrating the tissues of a healthy organism in an opportune place favorable for its germination.

It is evident that the more numerous the bacilli and the greater the facility of their discharge from the body of the leper, the more active and virulent the source of contagion. The tubercular leper, whose cutaneous tissues swarm with the bacilli and which are given off in myriads from the open surface of the broken-down tubercles, has undoubtedly a greater contagious activity than the anæsthetic leper in whom the bacilli are comparatively few and embedded deeply in the nerves from which they cannot readily find egress. It was formerly believed that the tubercular ulcerations from which the bacilli are discharged in myriads afforded the most prolific as well as the principal sources of infection. This view would imply a limitation of the danger to the period of ulceration, also that the anæsthetic leper is feebly or not at all contagious.

Recent bacteriological investigations, especially of leprous lesions of the mucous membranes, would seem to indicate the existence in these structures of possible sources of leprous contagion, the importance of which has been entirely overlooked or at least not sufficiently appreciated. The investigations of G. Sticker and of Jeanselme and Laurens on leprous lesions of the mucous membranes of the nose,

mouth, and larynx, the results of which were submitted to the Berlin Leprosy Congress (1897), must be regarded as among the most valuable of the recent contributions to our knowledge, as they tend to throw light upon an obscure chapter in the etiology of the disease. Notwithstanding the identification of the Hansen bacillus as the active pathogenic agent in leprosy, our knowledge of the sources of infection and the channels through which bacilli gain entrance to the system is by no means definite.

Several years ago before the above-mentioned investigations were undertaken, I insisted upon the precocity of the mucous-membrane manifestations of leprosy, asserting that in a majority of cases they were first determined toward the upper air passages, and I also maintained that the nasal and buccal secretions constituted the chief source of infection in leprosy.

Jeanselme and Laurens found leprous alterations in the nasal mucous membranes in sixteen out of twenty-six cases, or sixty per cent., of tubercular leprosy. These alterations, which were of the nature of a rhinitis, attended with coryza, obstruction of the nostrils, epistaxis, etc., constituted, they claimed, the first signs of the disease. The bacteriological examinations of the nasal secretions furnished facts of the greatest interest from a semeiological point of view. In the mucus of the leprous rhinitis, as in the blood of the epistaxis, Hansen's bacillus was abundantly found. In twelve cases it was possible to detect the specific bacilli at the first examination. Some of the cells were literally crowded with microorganisms having the morphological and microchemical characters of the lepra bacillus. In others the bacilli were extracellular and disseminated in the preparations, but they were always agglutinated in great numbers. It is worthy of note that the bacilli were also found in one case of anæsthetic leprosy.

These observers claim that: "The most important deduction to be made from these bacteriological examinations is that the nasal mucus of lepers is of very great virulence, and we do not believe that we extend legitimate inductions in affirming that rhinitis is one of the most effective sources in the propagation of leprosy. The contamination is effected all the more easily as the leper discharges a great number of bacilli in the initial period, when he does not suspect the nature of the malady and persons do not protect themselves from the disease.

"The same may be said of the leprous lesions of the mouth and throat, the nature of which is often not recognized, and which give off almost continually a multitude of bacilli."

Schaffer, of Breslau, demonstrated that vast numbers of bacilli left

the body by way of the diseased mucous membrane of the mouth and throat of the leper when reading aloud or talking. The number of bacilli projected would, of course, be still greater in the acts of sneezing and coughing. The importance of these facts from a prophylactic point of view is most interesting, and they coincide with what the present writer emphasized in an article several years ago: "In view of the fact that contamination probably takes place from the nasal and buccal secretions, these should be disinfected, etc., with the same scrupulous care as indicated in a case of tuberculosis."

The investigations of Sticker show that in the 153 cases examined by him evidences of the presence of bacilli in the secretions of the nasal mucous membranes were found in a large percentage of all the cases. Of these 153 cases, 58 were tubercular, 68 anæsthetic, and 27 mixed. Of the 58 tubercular cases, bacteriological examination showed the presence of bacilli in all but 2. Of the 68 anæsthetic cases, only 23 contained no bacilli, and of the 27 mixed cases, only 1 was free from bacilli. He concludes that the primary affection or its neighborhood in the nose is chiefly the origin from which the bacilli regularly and in enormous numbers are given off in the patient's proximity. Only the purulent sputum of a few lepers (22 out of 153) contained such enormous numbers of bacilli as the viscid or purulent secretion from the diseased nasal mucous membrane. Not even the suppurative nodules can compare with the above-named lesions in the spreading of the bacilli. Sticker believes that the nose continues to be an active focus for the projection of the bacilli during the entire course of the disease, even during the periods when the cutaneous manifestations have temporarily disappeared.

Physiological Secretions.—The physiological secretions may contain bacilli when the secretory structures are the seat of leprous changes, or they may serve as the vehicles of the virus. The saliva is loaded with bacilli when the leprous lesions are situated in the buccopharyngeal cavity. The bacillus has not been found in the urine, although the Chinese, according to Arning, think the urine is especially pathogenic.

Pathological Secretions.—The altered secretions of the nasal mucous membranes, the mucopus and blood, the discharges from broken-down nodules and ulcerating surfaces contain the bacilli in vast numbers. It is a question whether the pathological secretions in lepers of lesions not produced by leprosy contain the bacilli. It is claimed that the serous exudations of bullæ provoked by vesicatories upon the skin of lepers have been found to contain bacilli—a statement which is contested by other investigators. In addition to the sources of in-

fection already described, it is probable that every open wound or pathological break in the continuity of the skin may afford egress to the bacilli.

In advanced cases of tubercular leprosy the bacilli are able, according to Babes, to penetrate the follicular wall from within outward and reach the surface of the skin when the latter is still unbroken. It would appear that the opportunities for the escape of the bacilli from the body of the leper, and their transference directly or mediately to the bodies of healthy persons with whom he is brought in contact, are almost innumerable. The only explanation of why contamination takes place so rarely under such favoring conditions is that many of the bacilli are dead when discharged. Moreover, the bacillus lepræ seems to be a weak one, and, unless introduced in a tissue soil favorable for its growth, it does not germinate.

Heredity and Contagion.

A belief in the contagiousness and hereditary nature of leprosy has generally prevailed from the earliest ages until the present century. The early writers among the Arabians, Greeks, Hindoos, and others have recorded their belief in the contagiousness of leprosy, though differing as regards the manner in which it occurs. All the proscriptive measures for the suppression of leprosy formulated in the Levitical code, as well as measures for the isolation of lepers in leper houses enforced in mediæval times, were based upon the doctrine that the disease was contagious. The segregation of lepers in special hospitals and communities practised in many countries at the present day is based upon the conviction that every leper is a source of possible danger to those with whom he may come in contact.

The traditional belief that the disease was susceptible of hereditary transmission has never been questioned until comparatively recently. In all ages marriage between lepers has been prohibited or discountenanced by church and state. In mediæval times not only was it prohibited, but the development of the disease in one partner was regarded as a sufficient pretext, and even as an urgent argument, for the dissolution of the marriage tie. At the present day, in many countries where leprosy is endemic, the separation of the sexes in leper asylums and the interdiction of marriage between lepers is enforced by government authority.

Within the past half-century the doctrine of the contagiousness of leprosy began to be seriously contested. Daniellsen and Boeck, who were non-contagionists and were strong believers in heredity as the principal factor in the propagation of the disease, were largely influ-

ential in bringing about this change of opinion. In this view they were supported by the prestige and high authority of Virchow.

In 1867 the Royal College of Physicians of London promulgated the dogma that leprosy was non-contagious. "The all but unanimous conviction of the most experienced observers in different parts of the world is quite opposed to the view that leprosy is contagious or inoculable by proximity or contact with the disease. The evidence derived from the experience of attendants of leper asylums is especially conclusive on these points, the few accidents that have been reported in a contrary sense usually rest upon imperfect observation or they are recorded with so little attention to the necessary details as not to affect the above conclusion."

This opinion was generally accepted by the profession in Europe. As an evidence of how complete was the overthrow of the doctrine of contagion, it may be said that in 1885, when the famous discussion of the contagiousness of leprosy took place in the Paris Academy of Medicine, it appears that only three physicians in France upheld the doctrine of contagion.

With the elimination of what had been regarded as the principal factor in the acquisition of leprosy, it is not strange that the other factor was proportionately magnified in importance until it came to be believed that heredity was the principal agency in the propagation and production of the disease. According to many leprologists the influence of heredity was manifest not only in the direct line from parent to offspring, but collaterally as well. It was also held that it might skip over one or two generations and reappear in the descendants of lepers and that it might reappear in the second and fourth generations with greater force than in the first and third.

The sweeping assertion formulated by the Royal College of Physicians, that leprosy was non-contagious, was based largely upon negative facts of contagion while ignoring the equally numerous positive facts which testified to the contrary. Although the doctrine of contagion was generally abandoned in Europe, it was still upheld by many observers in countries where leprosy was endemic. A great amount of clinical evidence was accumulated showing a vast number of instances of individual and epidemic contagions. The development of new centres of leprosy in various parts of the world, the positive evidence that the disease never originated spontaneously, but was always imported by lepers, the insufficiency of heredity to explain the rapid spread of the disease, the observation of a large number of Europeans whose ascendants were free from all possible leprous contamination and in whom there could be no specific congenital predisposition, but who nevertheless developed the disease

after sojourning in countries where leprosy was endemic—all contributed to foster a growing scepticism in heredity as an important factor until professional opinion gradually came again to regard contagion as the principal factor in the propagation of the disease.

In 1887 the Royal College of Physicians modified its former decision by stating "the committee is quite aware that there is much difference of opinion respecting the communicability of leprosy, and that many colonial practitioners and inhabitants do not concur in the views expressed by the College in their report of 1867."

In 1889 the College reconsidered the whole question and practically recanted its earlier opinion in the statement "that there is undoubtedly, as the committee now admits, increasing evidence respecting the communicability of leprosy." It is worthy of note that in Norway and Sweden many of the former opponents of the doctrine of contagion have now become its most ardent advocates. From this review of the changes which medical opinion has undergone in reference to the mode of communication of leprosy, we can now examine more particularly into the question of the hereditary nature of the disease.

Is Leprosy Hereditary?

It is scarcely conceivable that a disease of so serious a nature and which so profoundly impresses the system should not exercise some influence upon the offspring. One recognized effect of leprosy, especially in the tubercular form, is its inhibitory influence upon the procreative power. This is doubtless due to the azoospermia which is especially marked in the advanced stage of the tubercular form, although the sterility of leprous marriages is not so pronounced as has been generally assumed. Clinical evidence would seem to show that the influence of leprous progenitors upon the offspring is scarcely appreciable in the early stage, but becomes manifest at a more advanced stage in the production of abortion, or of delicate children who die of infantile diarrhœa or succumb to various slight causes of disease. Abortion usually occurs at the third or fourth month, often without other assignable cause than fœtal cachexia, or the infant may be still-born at full term. In other cases the child is born living, but small, ill-developed, cachectic, and may succumb to athrepsia or degenerative changes.

It has been generally admitted that the leprogenic capacity of progenitors may be manifest in the transmission to the offspring of a constitutional protoplasmic state, expressed in a feeble organization and diminished capacity of resistance to the germs of disease in general. It is not settled, however, that there is transmitted a spe-

cific congenital predisposition to the germs of leprosy in particular. In an article already quoted I wrote: "As in the case of tuberculosis with which leprosy presents so many analogies, the influence of heredity is probably limited to the creation of a predisposition to the disease. This may be expressed in an abnormal susceptibility to the admission and pathogenic action of the bacilli due to a weak constitution and diminished capacity of resistance of the organism inherited from the leprous progenitor."

A more careful study of the question would seem to indicate that even this measure of influence accorded to leprous progenitors is a concession not warranted by the facts, since, as will be seen later, there would seem to be in the children of lepers a protective immunization against the disease, by the fact of the leprosy of the parents. The evidence which exists is hardly sufficient to establish an inherited specific predisposition to the germs of leprosy in particular. Besnier says that the predisposition of children of leprous parents to leprosy, if it exist, is certainly less accentuated, less particularized, and especially less characteristic than the predisposition of children of tuberculous parents to tuberculosis.

The question whether there is a direct transmission of leprosy from parents to offspring is still *sub judice*. From a scientific standpoint the acceptance of leprosy as a parasitic disease is hardly reconcilable with the theory that it is susceptible of transmission by the ovum or sperm cell. Hansen declares that a parasite cannot be transmitted by inheritance. "It may be handed on to the child by the parent, but in a different sense from the transmission of qualities primarily embraced in the sperm cell or germ cell. To speak of inherited infection is a contradiction in terms."

It is evident that the transmission of the germs of a disease by direct inheritance must take place by the sperm, the ovum, or through the uteroplacental circulation. There is no evidence that the bacilli find lodgment in the seminal cells, and from the comparative rarity of the bacilli in the ovary and in the female organs of generation, it is doubtful whether they are found in the ovum.

Besnier believes that in the rare cases in which direct inheritance is effected it is by the uteroplacental contamination of the fœtus. The lepra bacilli, he believes, may penetrate the placenta by way of the blood current. This mode of contagion he terms heredo-contagion. It must be remembered that the presence of the bacilli in the placenta or in the fœtus has never been demonstrated. The only recorded instance of an attempt to find bacilli in these structures was made by the writer, who secured the placenta, cord, and portions of the body of a child still-born at full term of leprous parents. Care-

ful repeated examinations of the specimen by Dr. Fordyce showed the entire absence of bacilli.

As regards the doctrine maintained by Zambaco Pacha and other leprologists, that the germs of leprosy may be inherited, but remain latent and appear only in later life (fifty-five to fifty-eight years) or reappear in succeeding generations, it may be said that it is entirely opposed to our knowledge of the laws of heredity and the pathogenic action of parasites. It involves the assumption that the pathogenic bacilli may remain inert in the organism for one or more generations and be transmitted conceptionally by the progenitors who are themselves uncontaminated. Hansen declares that the atavic transmission of physiological characters is not reproduced in the history of infective diseases. In discussing this question the Indian Leprosy Investigation Committee says: "In the study of embryological deformities, atavism may be of great importance, but if the term is employed to denote the sudden appearance of constitutional diseases after having skipped one or several generations it is inapplicable. Atavism has no place in the etiology of leprosy." It is to be noted that all alleged cases of atavic inheritance have been reported from countries where leprosy is endemic, with more or less numerous centres of infection, and where there were infinite chances of contagion from contact with lepers.

But independent of theoretical considerations the facts of observation show that heredity cannot be regarded as a prominent factor in the propagation of leprosy. A vast number of statistics have been collected from various sources in favor of the doctrine of heredity. Nothing shows more conclusively the misleading nature of statistics than the wrong interpretation which has been given to those bearing upon the question of heredity. The conclusions which are derived from a superficial or insufficient observation of certain facts are entirely traversed by the more careful study and a more intelligent interpretation of the same facts.

One or two sources of error to which statistics of this character are liable may be here pointed out. The defendants of the doctrine have been accustomed to class in the category of hereditary transmission all cases in which leprosy occurs in the descendants irrespective of the age at which the disease develops, while ignoring the multitudinous chances of infection from the leprous entourage.

It is well known that the early writers on syphilis grouped in the category of hereditary syphilis all cases occurring in infants. That they made no distinction between congenital and acquired infantile syphilis is evident from the fact that they speak of many children in whom the first infection occurs in the mouth or on the face, which

cases we now recognize as examples of the acquired form of the disease from nursing or otherwise. In the same way the advocates of heredity speak of all leprosy in children as inherited without eliminating the possibilities of post-natal contagion. Statistics show that the average age at which leprosy develops is from the twenty-fifth to the thirtieth year, and unless we concede an habitual latency of the germs during this prolonged period, it is evident that the disease in the average case is not transmitted by inheritance.

It may be admitted that leprosy is more common among the children of leprous parents than among those of healthy parentage, but this fact alone does not necessarily prove that the disease is inherited. Leprosy is essentially a family disease, not because it is hereditary, but because it is contagious and because in family life contagion more readily takes place. It may be restricted to one or several definite groups of families in a community for a long period, but the opportunities for postnatal infection in the thousand and one intimacies of family life cannot be ignored, and a closer study of these cases shows that the occurrence of leprosy among them is more reconcilable with the chances of accidental contamination than the theory of heredity.

The facts which may be invoked in favor of the non-hereditary character of the disease may be considered under the following heads:

(1) *Rarity of Congenital Leprosy.*—The exceeding rarity or complete default of cases of children born with leprous manifestations has been remarked by most observers. The testimony of careful and painstaking observers living in leprous countries, who have personally studied the disease in all its phases for years, is almost without exception to this effect.

Daniellsen and Boeck have never seen leprosy appear before the third or fifth year. They state that lepers have come to them saying that their children were born with spots or with bullæ of the extremities, appearing in the first months of life, but personally they have never seen a new-born child bearing leprous stigmata.

Leloir, in his extensive personal investigations of leprosy, never found a fœtus or new-born child affected. Out of 149 cases only 3 developed leprosy under ten years—at four, six, and eight years of age respectively. W. M. Jelly, in his investigations of leprosy in the Spanish provinces of Alicante and Valence, searched in vain for a leprous infant. He declares: "I have never seen or been able to find an exanthematous leprous baby or child." Falcao found in 709 cases only 3 as early as four years. The Leprosy Commission of India found in 2,371 cases only 49 as early as six years. Among the 6,000 or more cases observed in Hawaii, the youngest patient was three and one-half years old. In Cape Town, Africa, Impey states that of 1,088

cases in only 2 was the disease developed in children under five years of age, the youngest person contracting the disease being three years old. It would be easy to adduce testimony to the same effect from numerous other sources.

In the article to which reference has already been made I wrote: "There is no well-authenticated case of congenital leprosy on record. Navarro has reported a case of congenital leprosy which is apparently one of inherited syphilis. Two months subsequent to the child's birth the mother showed decisive signs of leprosy, as did also her daughter eight months later, and a daughter of three years died two years later; but as syphilis is by no means excluded, we are not bound even to accept this as a decided case of the hereditary transmission of leprosy."

In contravention of this statement the only observations which may be regarded as of a positive character are those of Zambaco Pacha, reported in his "Voyages chez les Lépreux." He admits that congenital leprosy appearing a short time after birth, some months or some days, is exceedingly rare. Sometimes one child in a family will be a leper, the others remaining unaffected, while in other cases one child may remain healthy while all the other children become lepers. He reports a number of cases in which children were born with undoubted manifestations of the disease. It is to be noted, however, that Zambaco Pacha denies the contagiousness of leprosy and accords the first place to heredity in the spread of the disease. He also denies the pathogenic rôle of Hansen's bacillus and asserts that to be born of leprous parents or to belong to an ethnical group in which leprosy is endemic would be sufficient evidence of heredity.

It will be seen that according to the testimony of the most competent observers leprosy is not manifested in the offspring until years after birth; very exceptionally as early as the third year, rarely before the fifth or sixth year, which would correspond to the classical period of incubation of the acquired disease. Even conceding the authenticity of Zambaco Pacha's cases of congenital leprosy, the proportion of such cases is infinitesimally small.

Age at which Leprosy Develops.—In quite a proportion of cases leprosy may be first evident at the age of puberty, from the twelfth to the fifteenth year, but in the immense majority of cases it does not develop before the thirtieth year of age. The clinical history of leprosy is more in accordance with the doctrine of contagion than with that of inherited transmission. The incidence of the disease in the children of leprous parents is in direct ratio to their exposure to the ordinary sources of contagion.

The evidence presented in favor of heredity has never been exclu-

sive of all possibilities of postnatal contagion. There is no case recorded of a new-born child promptly removed from all chances of contact with lepers, which later showed signs of the disease. In all cases of so-called heredity there is every reason to believe that if the children had been promptly removed from their leprous entourage, they would have escaped the infection. It was largely because of the commonly observed exemption of the offspring of lepers from the parental disease that the Kapiolani Home was established at Honolulu. The results of this practical scheme of separation show that if children are removed from exposure to contaminating contact at an early age, before postnatal infection takes place, they remain free from the disease.

The Comparative Rarity of a History of Leprous Antecedents.—Another argument which goes to show that the influence of heredity, if it exist, must be exceedingly restricted is the small proportion of cases in which there is a history of leprosy in the parents. According to Impey, there are at present (1896) in the Robben Island Asylum 520 lepers, of whom 475 were born of healthy parents; of the remaining 45 cases, the father alone was affected in 25, the mother in 16, and the father and mother both were diseased in only 4. Again there are 266 leper parents at the asylum who have had 951 children. Of these children 23 became leprous, which is less than 3 per cent. of the whole.

The comparatively small proportion of children (less than three per cent.) who became leprous would seem to indicate that the existence of leprosy in parents exercises upon the offspring a protective rather than a predisposing influence to the disease. We can scarcely conceive that, of an equal number of children born of healthy parents placed in this leprous environment and subjected to the numerous chances of contamination incident to the intimate contact of family life, only three per cent. would escape. Whether there has been in these children a "vaccinatory immunization," as it has been termed, or whether there is a greater resisting power in the tissues of children against the lepra germs cannot be determined. The assertion that the lepra bacilli may lie latent for a long time in children and not develop until individual resistance is lowered is purely hypothetical. Certainly these facts do not tend to favor the theory of a specific predisposition to the disease.

The statistics of the Almora Asylum in India may be referred to. Of 14 children who had been admitted, 1 had died; a girl of twenty-two had married and had children to all appearances healthy. Of the remaining 12, 7 were born in the asylum, of two leper parents, and 5 were the offspring of parents, both lepers.

They were in excellent health and showed no signs of leprosy. At Crete, Carter found that among 88 grown-up children of lepers, several thirty years of age, only 6 per cent. were leprous. Bracken reports that of 34 Norwegian lepers who had emigrated to this country, 21 are known to have been married—15 men and 6 women. These marriages have resulted in 78 children, not one of whom show signs of the parental disease. Hansen, who in 1891 made a tour of investigation in the Scandinavian colonies of North America, found that of the descendants of 168 lepers who had emigrated from Norway to this country, not one had become a leper. Dr. Brockman estimates that there must be in Minnesota alone 100,000 persons with leprous ancestors of Norwegian descent, direct and collateral, yet leprosy has never appeared among them. My examination of numerous lepers in Mexico failed to reveal the history of hereditary taint in a single individual.

Spread of Epidemics.—The history of leprosy in the Sandwich Islands and other endemic centres shows conclusively that the rapid increase in the number of lepers is vastly disproportionate to the number of births among lepers. Sterility is a common result of marriages among Hawaiian lepers. Only five children were born in the leper settlement of Molokai within ten years, although no restriction was placed upon the intermarriage of lepers. In 1886 Mouritz collected statistics of twenty-six children born in the leper settlement, whose ages ranged from three to fourteen years. Seventeen of these showed no sign of the disease. All of these children lived under the most favorable conditions that could be conceived for contracting the disease, and it is altogether probable that if the nine who became infected had been removed from contact with their leprous parents at an early age they would have escaped the disease.

In tracing the development and spread of leprosy in the Sandwich Islands, a careful study of the facts shows that heredity cannot be considered an important factor. According to the most authentic accounts the first case of leprosy was observed about 1846. Twenty years later several hundred lepers were sent to the leper settlement, a large proportion of whom must have been born years before leprosy was introduced into the islands.

When we consider that over six thousand lepers have been consigned to this leper settlement since its establishment, it is evident that only a very small contingent could have been the offspring of leper parents.

Finally may be noted the numerous cases in which heredity is impossible, shown by the fact that Europeans who have lived in countries which have been free from leprosy for centuries, and in

whom by no possibility could a hereditary taint be alleged, acquire the disease when sojourning in countries in which leprosy prevails.

Another argument may be drawn from the historical fact that the Chinese have spread leprosy through the greater part of the Indian Archipelago, Oceanica, and the islands of the Pacific. The many natives and foreigners who have contracted the disease are not of Mongolian descent.

Is Leprosy Contagious?

As before intimated in reviewing the change which medical opinion has undergone in reference to the etiology of leprosy, the doctrine of its contagiousness has within recent years regained the ascendency and this is now generally regarded as the principal factor in the propagation of the disease.

The discovery of a specific bacterium which is invariably and exclusively found in the bodies of lepers, and which can be brought into causal relation with every manifestation of the disease, gave a new aspect to the question of contagiousness. Even before the demonstration of the constant presence of the bacillus lepræ in the anatomical elements and secretions of the leprous subject there was abundant clinical evidence of the communicability of the disease. The facts of observation, as well as analogies with other diseases admittedly contagious, rendered it difficult to conceive how a disease so specific in its characteristics could develop without a specific cause. Bacteriological research simply confirmed what clinical evidence had already demonstrated.

The contagiousness of leprosy would seem to be a necessary corollary of the demonstration of its parasitic nature. The existence of a specific bacillus is not, however, accepted by all as convincing proof that it is the pathogenic agent and that it is transferred directly by contact of a leper with a healthy person. The only link wanting in the chain of direct evidence is that the *modus operandi* of contagion, the actual transference of the bacillus from one person to another, does not admit of positive demonstration. The circumstantial evidence is sufficiently complete. An individual affected with leprosy in whose lesions the bacilli are found comes into more or less intimate and prolonged contact with a healthy person free from these germs. By and by the latter shows symptoms which indicate that he has been the recipient of the germs of the former—he becomes leprous. It is evident that in some way or manner the germs from the diseased person have passed into the healthy organism and infected it. This infection takes place under certain well-fixed laws and conditions which are doubtless peculiar to the leprous process.

It is probable that the mode of contagion of every bacillary disease has an individuality of its own, depending partly upon the germinative qualities of the bacilli causing the disease and partly upon the soil that these organisms require for their development and the completion of their cycles of life.

Whether, as has been suggested, the lepra bacillus undergoes an evolutionary change outside the human body in some intermediary host before it becomes endowed with a germinative capacity when brought in contact with human tissues is immaterial to the present inquiry. The hypothesis of an intermediary host does not alter the fact that the bacillus which comes from the leper's body is the essential agent of contagion.

Instances of Contagion.—The literature of leprosy abounds with well-authenticated cases of individual contagions, showing in the clearest and most positive manner that the disease spreads from leprous to healthy persons by contact. Thin, in his work on "Leprosy" (page 141 *et seq.*), has quoted more than sixty well-authenticated observations tracing directly the communication of the disease from lepers to previously healthy persons by individual contact or in family life. A few of these cases may be here given:

At Grenada, a girl, aged about twelve to fourteen, slept in the same bed with a young woman who had symptoms of leprosy. Within twelve months the girl had a leprous rash, and was a confirmed leper seven or eight years afterwards. The mother of this girl contracted the disease; the father escaped.

A healthy girl, aged seven, slept in the same bed with a boy, aged nine, who was leprous, and she became affected with leprosy.

Dr. Davy cites the case, on the authority of the medical officer of Trinidad Hospital, of a man who became a leper after two children had been born to him. Afterwards these children became leprous.

A European officer in India became leprous when he was forty-five, and within two years had developed the full stage of tubercular leprosy. His large family and many relations, as well as parents, were perfectly healthy.

A boy lived with an apothecary who was a leper, and became leprous. A convict, acting as orderly to the same apothecary, became affected with the disease and died within a year of the first appearance of the affection.

A European, who was a leper, stated that he had contracted the disease from a favorite servant who was constantly about his person.

A child whose parents, grandparents, and four brothers and sisters were healthy was the favorite of a leper, the brother of his grand-

father, and frequently slept in the same bed with him. He became affected with leprosy.

A woman in whose family it was known that for three generations there was no leprosy was sent when a child to Eze, County of Nice, to be wet-nursed by a woman who appeared to be healthy, but in whose family there had been cases of leprosy. On the woman herself, immediately after the child was weaned, leprous manifestations were observed. The child grew up and became leprous in mature years. She married and had four children. Her husband and two daughters, who died young, had no leprosy. The other two children (sons) have since died lepers. Of these sons there is the following history: One developed symptoms of leprosy when doing his military service, after having left Eze. He died, aged twenty-eight, of leprosy. His brother died of leprosy at fifty. His wife still lives and is well. He had been long in intimate relations with a woman who came from the north of France, and who belonged to a family in which there was no leprosy. This woman and one of her sons, who had been much associated with the man, became leprous three years after he showed symptoms of the disease.

A family named Quin, consisting of a father, mother, and five children, all in good health and free from leprous taint, left Nice for St. Laurent d'Eze. There they associated daily with a family of lepers. They had meals in common and *slept on straw in the same granary*. After six years of this intimacy leprosy appeared in the family of Quin. The mother and five children successively died of leprosy, and the father has just died of leprosy in the hospital at Nice.

The village of Turette, situated on the right bank of the Paillon river of Nice, was free from leprosy until 1815. At that time a family Mas—— took a servant who was a leper. From this patient leprosy was conveyed gradually to nine persons. The household Mas——, husband and wife, were attacked first; then a family Gar——, who had frequent relations with the Mas——. A cousin of the Gar—— family, who lived with them, was also affected, as well as his wife. His three children still live at Tourette, and are lepers. One of the latter, having long lived in a shepherd's hut, made a present of the cabin in which he had slept to a shepherd belonging to a healthy family. This shepherd lived in the cabin for a long time. He is now a leper.

According to Simond, quoted by Forne, fourteen convicts, transported to Guiana, thirteen of whom were born in France and one in Algiers, became leprous after they were set free.

A Sister of Mercy, born in France of healthy parents, and who

had excellent health until she was forty-six years of age, came to French Guiana in 1862. Five years after her arrival there she became attached to the service of the lazaretto of Acarouany, where she was occupied in attending to lepers in various ways. In 1878, at the age of forty-six, after having been eleven years in the lazaretto, she experienced the first symptoms of leprosy, and in 1883 was in the last stage of the disease. She believed she had been infected by washing linen belonging to leper women; but Dr. Hulin de Godon stated that the Sister became leprous after having pricked her fingers with a needle, which she had used in sewing lepers' clothes.

A European Sister of Mercy, free from hereditary taint, who was occupied in the linen room of the hospital at Tahiti, inoculated herself with a sewing-needle under the same condition as the Sister at Guiana. Se was sent home to France, in 1885, a leper.

A European child, nine years old, free from taint, associated with a leprous colored child. During their play the leprous child took a pin or penknife and thrust it into the anæsthetic skin of his leg without experiencing pain. The astonished white child repeated the experiment on himself, causing severe pain. He was afterwards sent to Holland to be educated, and returned, when nineteen years old, to Java, a confirmed leper, the disease having appeared two years before his return. The gentleman was well known in Batavia, and the case was clearly either one of contagion or inoculation.

Sir William Moore relates that when he was stationed in India he had the patients (some of whom suffered from leprosy) who were affected with itch rubbed with sulphur ointment at the dispensary. One of the persons employed to do this injured her hand and afterwards developed leprosy, her family being quite free from the malady, and no history of other association with lepers being obtainable.

Prof. Cayley relates that, in 1886, the leper ward at Burdwan jail contained about thirty lepers. During the twelve months that he was in charge of the jail two persons who had been there four or five years, and who were selected as healthy men, were put in charge of the leper ward and were attacked with leprosy.

A white girl, aged fifteen, of good family, without leprosy taint, accepted an invitation from a young friend, members of whose family were lepers, the fact being concealed. The girls slept in the same bed, and lived intimately together. After three months the girl belonging to the leprous family left her friends, and some time afterwards the disease made its appearance. The girl who was invited grew up to womanhood, married, and had children; but after a few years the disease attacked her, and she died a leper.

A boy belonging to a clean family used to play and sleep with a

boy who belonged to a family in which there was leprosy. The tainted boy soon became a leper, and three years afterwards his playfellow, in whose family there was taint, became leprous.

A white man, aged twenty-five, was on intimate terms and slept with a young man who had leprous spots. In the course of about a year the previously clean man found spots on his person, and died in a short time of leprosy. His family was and remained free from all taint.

A young colored boy, of clean family, while suffering from an eruption, played with a boy who was a leper and had a suppurating ulcer in the foot. The previously healthy boy became a leper about a year afterwards, his family remaining untainted.

A young Scotchman, whose parents had never left Europe, was contaminated by a leper woman. Within ten months he developed leprous spots and died a leper.

A colored man, a leper of Kaoo Island, stated that he attributed his disease to the fact that his mother washed the clothes of several lepers and used to wash his along with them. He stated that his parents and relations, so far as he knew, were free from leprosy.

Dr. Liveing relates that a soldier who had served in India died in Guernsey, and that in his last illness he had sores on his fingers and toes, an enlargement of the nose, and discoloration on the skin of the face. One of this man's sons, when fifteen years old, developed leprosy.

The only case except that of Dr. Hawtrey Benson that we have found recorded, in which the disease must have been communicated in England, is that published in Guy's Hospital Reports for 1868, and referred to by Munro. Johanna Crawley, an Irishwoman, aged thirty-four, had lived thirty years at Stepney. In 1866 she had lost part of the first finger of the right hand. On her body and limbs were large brown patches, and there was decided anæsthesia as far up as the elbows. The face was puffy, the lips and ears were swollen. Munro saw her daughter at Stepney, a woman aged twenty-five, and was informed by her that Johanna died in 1874, after losing part of all her fingers and toes, the blisters and destruction of bone causing great pain.

A widow, aged fifty-eight, with several children, went to live with a daughter who was a leper, and was attacked five years afterwards when she was sixty-five years of age.

In St. Kitts, Hannah Carty, when a girl, slept with and washed the clothes of T. Wilson, who was covered with leprous sores. She was attacked at the age of seventeen. Her family were all healthy.

Epidemic and Endemic Contagions.—When leprosy invades a new

country or a community, which is but an aggregation of individuals, the same mode of contagion is manifest. It spreads from individual to individual by proximity or contact. The primary essential condition of the development of leprosy in a country or race previously exempt is the importation of leprous germs in the body of a leper who becomes a centre of contagion, and creates new foci of the disease around him. The disease spreads more or less rapidly, assuming epidemic proportions or becoming circumscribed in small endemic foci according as the conditions are more or less favorable. When introduced into a virgin soil, as in the Sandwich Islands for example, where the racial susceptibility to disease is marked and the conditions for its multiplication are favored by promiscuity in the habits of eating, drinking, and sleeping, and where free and intimate contact with the leper is restrained by no wholesome fear of the disease, it spreads with extraordinary rapidity and shows all the characteristics of a virulent epidemic.

When imported into countries of advanced civilization, in the United States or Central Europe for example, where the physical stamina is of a higher order, where the rules of personal hygiene and sanitary living are observed, and where public sentiment or popular prejudice looks upon the leper as the bearer of a deadly contagion to be shunned and avoided, leprosy rarely spreads, and contagion can scarcely be said to exist.

In countries where leprosy has been endemic or maintained in permanence for generations or centuries it will be found that its limitation or spread is largely influenced by the more or less free contact of the leprous with the healthy. Where public opinion has inculcated a wholesome dread of the disease or where governmental authority has taken measures of isolation and protection the disease is circumscribed and limited; in countries where neither law nor public opinion prevents the free intermingling of lepers with the healthy of the community the disease spreads.

In India, Mr. McNamara says: "Although lepers move about among their countrymen, they are to a great extent isolated from them. Who ever saw a healthy native touch, much less eat with, one afflicted with leprosy? In many parts of India the fact of admitting a leper to a general hospital is sufficient to drive every other person out of it. The wealthy leper may purchase immunity from some of the social evils to which his poorer brethren are exposed; but even he is frequently obliged to leave house and home and wander as an outcast over the face of the earth, visiting shrines and holy places in expiation of his sins which he believes have been punished by the infliction of leprosy. Rich and poor lepers, however, though

living and moving among their fellow-men, are as isolated from them as were those condemned to the lazar houses in the Middle Ages.

Of interest in this connection are Vandyke Carter's observations of the method of dissemination of leprosy in India. "Taking the more infected districts, we find that while much of the surface is covered by disease, yet the leper villages are not indiscriminately scattered. Thus the chief town always represents a chief 'focus'; next the villages immediately around are affected, and beyond these pass off, as it were, lines of leper localities in various directions which may meet and blend or become continuous with similar lines in adjoining districts. At present I find hardly a single instance in which a leper village does not form either a focus or a part of lines or groups such as those now mentioned. No leper village is found to be isolated; all are connected with others immediately adjoining, the rare uninfected intervening villages being temporary or incidental exceptions. All these data may be said to point to transmission of the leprous disease by human intercourse—that is, by contagion."

The opponents of contagion base their belief largely upon the failure of all attempts to inoculate the disease, the observations of numerous persons who have lived in prolonged contact with lepers without having contracted the disease, as for example physicians, Sisters of Charity, nurses, and attendants who have come in contact with lepers in hospitals, the comparative infrequency of conjugal contamination, the failure of leprosy to spread when imported into certain countries, and finally the fact that leprosy does not comport itself as a contagious disease. These objections may be considered in detail.

Failure of Inoculation Experiments in Animals.—The result of experimental attempts in inoculating animals is a record of failures simply because leprosy is an exclusively human disease. The tissues of the human species furnish a culture soil favorable to the reception and development of the pathogenic agent, while the tissues of animals are immune.

The proposition, that because a disease cannot be inoculated in animals, it therefore cannot be transmitted from man to man, would be equivalent to a denial of the contagious nature of many diseases admittedly contagious. There is no well-authenticated proof of the inoculation in animals of syphilis, which may be considered the type of an inoculable disease. Besides, all experience shows that nothing is more difficult than inoculating animals with human diseases. The failure may in many instances be due to our ignorance of the precise conditions which determine the vegetability of disease germs. As is well known, the earlier attempts to inoculate the products of tuberculosis were failures.

Failure of Attempts to Inoculate Man.—While the results of these experiments, which are elsewhere referred to in detail, were simply negative, they cannot be considered absolutely demonstrative of the impossibility of inoculating leprosy in man. It must be remembered that they were undertaken at a period when the bacteriology of the disease was unknown, and with no attention to technical details which are now deemed essential in experimental inquiry, or it is possible that the systems of the healthy, well-fed individuals who were subjected to experiment were not in a condition to conceive and develop the pathogenic action of the bacilli. As Besnier suggests, "one should not forget that the insuccess of an inoculation often depends upon the ignorance of the experimental conditions attached to the special mode of contagiosity peculiar to the affection"; further, "if experiments upon man were lawful at the present day, absolute demonstration would not be long in forthcoming." The only case in which inoculation from man to man was claimed to be successful was that of Keanu, elsewhere referred to.

Unless we single out leprosy as an exception to other infectious diseases, the negative facts of inoculation experiments cannot be considered proofs of its non-contagiousness. It is well known that the germs of diphtheria, scarlatina, cholera, typhoid fever, etc., have never been inoculated in man, but this negative evidence cannot be considered as proof of their non-infectious character.

Reference might be made to the repeated attempts to inoculate favus in man and the uniform failure of all the earlier attempts to transfer the disease from one host to another. The question of vaccination leprosy has an important bearing upon the determination of the possibility of inoculating the disease and will be considered later in connection with the modes of infection.

My own belief is that leprosy is inoculable in man, and that we have abundant clinical proof that accidental inoculations play an important rôle in the introduction of the germs.

Rarity of Conjugal Contamination.—The concurrent testimony of many observers in various parts of the world where leprosy is endemic shows that when one partner of a marriage is a leper the incidence of the disease in the other partner is surprisingly small, on the assumption that contagion takes place from intimate contact. Besnier disposes of the whole question, especially of the cases in which a healthy woman has borne children to a leprous man while she herself shows no signs of the disease, on the ground that the immunity of the woman is not a fact of non-contamination, but a fact of conceptional immunization comparable to what is realized in conceptional syphilis, as formulated in the law of Colles. It may be urged against this in-

terpretation that it takes no account of the equally large and perhaps larger number of cases in which a healthy man is married to a leprous woman, or has relations with numerous leper women, without being contaminated.

I have reported the case of a Hawaiian who had been the husband of a leprous woman for twenty-nine years, two daughters of this union both being leprous, while he remained absolutely free from all signs of the disease. This was probably a case illustrating absolute immunity, as the entire family lived in the leper settlement, and the opportunities for extra-conjugal contagion were numerous. Many instances of similar character came under my observation, as my attention was particularly directed to this class of cases, since they were in opposition to the opinion which generally prevailed among the physicians, as well as the laity, of Hawaii, that the disease was commonly propagated by sexual intercourse.

An explanation, though in my opinion an insufficient one, of this frequent immunity from marital contagion has been sought in the fact that the age at which lepers marry corresponds to a period in which the susceptibility to the disease is markedly diminished. An analysis of a large number of cases shows that the susceptibility to the disease is particularly marked from the twentieth to the thirtieth year. After the thirtieth year the tendency progressively decreases, so that leprosy is apt to attack the man before the age of marriage, and as it often saps the virility, especially in tubercular cases, the wife incurs no additional risk to that of any other person in contact with a leper. It is claimed that "when leprosy occurs after marriage, by the time the man is able to communicate the disease his wife has from her age become in most cases insusceptible."

Too much importance should not be attached to explanations of this nature, as observations prove most conclusively that leprous contamination in marriage is by no means uncommon. It must be remembered that in its mode of contagion leprosy resembles tuberculosis rather than syphilis. It is a matter of general observation that consumption, an admittedly contagious disease, is rarely marital, while syphilis is almost always shared with the partner in marriage.

A few of the numerous cases recorded in literature which show in the most positive manner that the wife or husband has contracted the disease from the other during marriage may be here quoted.

The following cases are taken from the reports to the Government of India and other well-authenticated sources ("Leprosy," Thin, pp. 139 *et seq.*):

A girl, in whose family there was no trace of leprosy, married a leper, and after some years became leprous.

A sweeper, who belonged to a family in which there was no leprosy, married a leper woman, and himself became a leper.

A weaver, whose father and elder sister were lepers, became leprous at thirty. His wife continued to live with him and eventually became a leper.

A weaver became a leper at forty-five. His wife continued to live with him and became leprous.

A cultivator became leprous at forty-eight. His wife became affected with leprosy a year later.

A man became a leper at thirty-two, his brother being a leper. His wife lived with him for two years afterwards and became leprous.

A woman, whose grandfather and father were lepers, became a leper at twenty-eight. Her husband, who lived with her a year afterwards, became affected.

A sweeper became a leper at eighteen, and his wife was afterwards affected.

A woman, whose father died of leprosy, became affected, and her husband developed leprosy the following year.

Deputy Surgeon-General Cockburn states that he had seen a wife with her two children contract the disease by remaining with her husband, who was affected by it, while three other children who left him remained free.

Greene states that he has seen several instances at Sehampore Hospital in which the disease was acquired by sexual intercourse.

Ghose relates a case of a woman who became leprous after her husband. When he died, she went to live with her brother, and within a year the brother acquired leprosy. In the course of six years three other individuals in neighboring houses got the disease. Ghose was assured that before this woman returned home after her husband's death there had not been a leper in that village.

Van Holst relates the case of an officer in Dutch Guiana who contracted leprosy from cohabiting with a woman whose family were affected with the disease.

Two instances at Corfu are related in which the wives became leprous some years after the husbands.

At Mauritius, a case is related in which a wife became affected after her husband, and another in which, after a man became a leper, the child of his wife by a former husband became affected.

An Englishman in British Guiana cohabited with a colored woman and became leprous. The woman had not been suspected of leprosy, although afterwards it was found that she had had the spots on her body previously. One of her sisters was leprous, and the woman's child, when five years old, exhibited signs of the disease.

A white man, aged twenty-five, became a leper after sleeping in the same bed and using the same pipe with a leper.

A man, soon after the birth of his first child, discovered that his wife was a leper, and shortly afterwards became one himself. His children remained free.

A girl belonging to a leprous family of Laghet left her home when twelve years of age and became a servant at Nice. When she was twenty-two, and in perfect health, she married a healthy, strong young man from the north of France. She was nineteen years old when her father first showed signs of leprosy. When she was twenty-seven years old she had leprous tubercles below the left breast, and died at the age of thirty at the hospital at Nice. Two years after the death of his wife the husband showed leprous development in the face, and died of the disease three years later.

An Englishman, whose parents never left Europe, lived with a woman who some time afterwards showed symptoms of leprosy. The man became a leper and was seen by the commission.

A white man, aged thirty-five, born in England, cohabited with a colored woman who was leprous without the fact being known. He became a leper and died of the disease in Europe.

Munro also quotes Schilling to the effect that he could point out many examples of husbands and wives contracting the disease during marriage "did shame permit."

Rarity of Contamination of Physicians, Nurses, and Others who Care for Lepers.—The argument of the Royal College of Physicians against the contagiousness of leprosy was chiefly based upon data of this nature, viz., "the evidence derived from the experience of attendants in leper asylums is especially conclusive upon this point."

The same argument might be employed against the contagiousness of syphilis, tuberculosis, etc. During his long service at the Brompton Hospital for Consumptives Williams declares that he has observed only three or four cases of contagion among the *personnel* of the hospital.

In the great establishments for consumptives at Görbersdorf, in Germany, which have received twenty-five thousand patients within forty years, the mortality among the attendants, who are taken from an outdoor to an indoor life, is very low in spite of most exhausting work.

The immunity against leprosy is no more remarkable than that exhibited by the attendants upon consumptive patients. In general hospitals where tuberculous patients are received without being isolated, as well as in special sanatoria for this class of patients, the rarity or absence of transmission of the disease is a matter of common observation.

In my observation of more than fifteen years in the venereal wards of the Charity Hospital of this city I have known of but two physicians who have contracted syphilis from contact with patients in this service. Within the same period I have been consulted by twenty times that number of medical men who have contracted syphilis in family practice, surgical and obstetrical. It is a noteworthy fact that specialists in venereal disease who are most exposed to contact with syphilis are rarely contaminated, because they recognize the possible dangers and take greater precautions against infection, while those engaged in family practice are not impressed with a recognition of the risks incurred and the necessity of great circumspection in the examination of patients of whose possible syphilitic history and antecedents they know nothing.

Neve has suggested the possibility of immunity to the infection of leprosy being acquired by habituation. "We know that a pathologist engaged in constant post-mortem work enjoys a freedom from accidental blood poisoning not shared by those fresh to the work. The surgeon who frequently attends cases of infectious disease appears to become similarly protected. Does living in contact with leprosy ever produce a like immunity?"

Physicians who care for lepers in hospitals and asylums are quite as liable to contract leprosy as others who are equally exposed. The reason why they commonly escape contamination is because simple measures of precaution and disinfection and the intelligent avoidance of intimate contact reduce the chances of contagion to a minimum. But even with all the precautions which may be taken the exemption of physicians is not nearly so complete as has been pretended. We are obliged to admit professional leprosy as well as professional syphilis.

Vidal has reported the case of a Brazilian doctor who attended lepers and became himself a leper. Some years ago Dr. X—— from South America, who had attended lepers in his country, came under my observation for leprosy. Miss C——, of Ohio, a medical missionary, who attended on lepers in India, consulted me on her return to this country and was found to be suffering from leprosy. I have information of three physicians who contracted leprosy in Hawaii. "Schilling, McNamara, Lander, Hillebrand, Robertson, Livingston, Carter, Pasquier, and many others have published cases of attendants on lepers and even doctors themselves who have been after a time attacked by the disease" (Leloir).

Numerous cases are recorded of Sisters of Charity and nurses who have contracted leprosy in caring for the sick in asylums and hospitals. The proportion of the Kohuas or helpers in the leper settle-

ment of Molokai who become contaminated is from nine to ten per cent.

As conspicuous examples of priests who have, in attending upon lepers, contracted the disease, may be mentioned Father Baglioli, who attended lepers in the Charity Hospital of New Orleans, and remembers giving extreme unction to two of them, rubbing their hands with oil during the administration of the rites. In his case the first symptom was swelling of the mucous membrane of the nostrils. The case of Father Damien, which was long cited as an example of the non-contagiousness of leprosy, although he finally succumbed to the disease, is too well known to require more than mention. Undoubtedly the proportion of attendants upon lepers who contract the disease is much larger than is generally supposed. Prolonged exemption does not guarantee a continued immunity.

A case which has been frequently cited as a proof of the non-contagiousness of the disease was that of the washerwoman of the Leper Hospital of Molokai who had washed the soiled clothing of the worst patients for seventeen years. In addition she had lived with two leper husbands in succession, and yet she had remained hale, hearty, and apparently healthy during all this period. Upon the occasion of my first visit to the leper settlement in 1889 I found that this woman was suffering from undoubted manifestations of the disease.

Several years ago I instanced the case of Mr. D——, who had lived for nine years in the leper settlement of Molokai in daily and intimate contact with lepers—his principal work being the dressing of leprous sores and ulcers, sometimes attending to one hundred and fifty a day—as a notable example of immunity against contagion. Quite recently it has transpired that he, too, has become a leper.

Leprosy Imported into Certain Countries does not Spread.—Conclusions as to the interpretation of this fact and its bearing upon the contagiousness of leprosy will depend largely upon the point of view from which the question is envisaged. If the observer limits his field of examination and judgment to certain parts of Europe and the United States, he may find little clinical evidence of the active spread of leprosy by contagion. Observation shows that leprous germs introduced into these favored regions do not take root and spread; they rarely survive the death of the leper.

In New York, for example, large numbers of lepers coming from countries where leprosy is endemic have lived for years, many of them have been sent to general hospitals where they have died, and yet so far as is known no case of indigenous leprosy can be traced to association or contact with these patients. The same experience has been noted in London, Paris, and Berlin, where lepers from other

countries have flocked for treatment and have been received in the general hospitals without special measures of isolation, and yet no case of leprous contamination has been traced to contact with them.

If, however, the field of observation be somewhat enlarged, embracing the whole of Europe and the United States, it will be found that while in certain regions the disease when introduced does not spread, but rather tends to die out from natural causes, yet in other regions leprosy exhibits the unmistakable characters of a contagious disease.

For more than fifty years there has existed in Northern Europe an active and important centre of leprosy which spread more or less rapidly during a certain period until it assumed epidemic proportions, but which is now fortunately in process of extinction. Equally conclusive evidence may be found in the development of endemic foci in Parcente, Alicante, and other provinces in Spain, and of small isolated epidemics in other parts of Europe.

In the United States we find the same apparent anomalies or paradoxes of leprous contagion. Thus one hundred and sixty Norwegian leper immigrants have settled in the Scandinavian colonies of our Northwestern States, and their histories have been followed up, yet there has not been a single case of contamination (with the possible exception of one case reported by Dr. Hoegh) traced to contact with these imported lepers. Almost all of them have died and the seeds of the disease have perished with them.

If now we turn our attention to the more tropical region of our Southern seaboard, we shall find that there has been in Louisiana a notable and alarming increase in leprosy, and that within the past twenty-five years it has spread so rapidly as to prove a serious menace to the public health. A remarkable feature of the Louisiana epidemic is that the disease had formerly existed there during colonial times, had become practically extinct, and after nearly a century of silence and repose has reawakened into activity.

On the other hand, if one takes a broad and general survey of leprosy in all ages and in all countries, there is found the most abundant and conclusive evidence that the disease, when introduced into a community or country previously exempt, always spreads when the conditions are favorable. The history of leprosy is one continuous illustration of local and general epidemics originating from the incoming of foreign lepers into non-infected countries.

The study of the disease in small circumscribed leprosy areas with a fixed population, where the state of health of the different families has been known for a long period, shows that its development may al-

ways be traced to the introduction of a leper, and its spread is determined altogether by conditions of promiscuity and intimate contact.

The outbreak of leprosy in a new country or a non-infected race can always be traced to the immigration of lepers. The facts of the development and spread of leprosy in the Sandwich Islands furnish the most conclusive proof of its contagiousness. Upon no other possible ground can be explained the remarkably rapid dissemination of the disease which in the space of a single generation decimated the native population of these islands. It is estimated that at the present day from five to ten per cent. of the entire native population is affected with the disease, while many foreigners coming from countries where leprosy is not endemic and free from leprous antecedents have become infected. The number of such cases is already over one hundred, exclusive of the Chinese, Japanese, Portuguese, and South Sea Islanders.

Practically we find that in leprous countries, where the observer has the opportunity of studying the disease at close range and in all its phases, there is little scepticism as to its contagiousness, while in non-leprous countries, especially where the observer bases his judgment upon a superficial and limited observation, doubt begins to enter.

Leprosy does not Comport Itself as a Contagious Disease.—Finally there remains to be considered the objection to the doctrine of contagion which is based upon the exceeding variability of the contagious power of leprosy, and the observation that under certain conditions this characteristic is doubtful or fails altogether, or, at any rate, is not exhibited with that uniformity and constancy which one would naturally expect in a communicable disease.

It is claimed if leprosy is contracted always and only from the leper that, whenever the necessary conditions—the presence of a leper and proximity or contact with healthy persons—coexist, infection should take place. This objection, however, loses its importance when it is considered that each infectious disease has a contagious mode peculiar to itself, dependent partly upon the life conditions of the individual germ and partly upon the favorable or counteracting qualities of the soil in which it is implanted.

It would be illogical to assume that the contagious mode of a chronic infectious disease, like leprosy, of long incubation and sluggish evolution should conform in every particular to that of an acute infectious disease with a short incubation in which the phenomena succeed each other with great rapidity, like smallpox, for example. And yet many physicians deny the contagiousness of leprosy because it cannot be demonstrated that it is contagious in the same manner

or in the same degree of intensity as smallpox or even syphilis. It may be admitted that the evidence of contagion in these diseases is more positive and direct than in the case of leprosy. The intensity of the contagious activity of the two diseases mentioned and the receptivity of the human organism are so pronounced that contagion is effected almost invariably when the conditions of infectious or inoculative contact exist.

If, however, we compare leprosy with tuberculosis, we can trace numerous analogies in their contagious modes. We find the same apparent anomalies and paradoxes of contagion, due to the variable virulence of their respective germs under different conditions. The contagion of tuberculosis is not constant or invariable, but contingent upon the constitutional state and individual resistance of the recipient. The most intimate and prolonged contact with a consumptive is not necessarily followed by infection. Marital contamination is rare in tuberculosis. Climate and other conditions exert an inhibitory influence not only upon the development of the disease, but also upon its contagious activity. Tuberculosis is contagious in certain regions, feebly or not at all so in others.

The contagiousness of tuberculosis has been established not only by clinical facts, but by successful cultures and inoculations of the tubercle bacillus. The bacillus lepræ has not been successfully cultivated, and experimental inquiry has thrown no light upon its modes of growth and manner of reproduction. But while we are ignorant of the exact conditions under which the pathogenic agent of leprosy is best able to maintain and perpetuate its existence, observation shows conclusively that the surroundings which man acquires in certain localities are destructive of the microbes, while in other localities the conditions which surround man favor their preservation and propagation.

Van Dyke Carter remarks, apropos of this aspect of the question, that "the direct communication of disease is hedged around also by modifying influences belonging to both giver and taker, and these influences are so powerful and complex that the event in question—contagion—becomes to be regarded by many as a matter of doubt."

Further, it may be said that the "variable virulence," as it has been termed, of leprous contagion at different epochs and in different countries is no more remarkable than that exhibited by other diseases. Its development and decline, its exacerbations and subsidences, and its resurrection in certain countries after long periods of silence and apparent extinction are paralleled in the history of other diseases. The epidemic of leprosy which devastated Europe during the Middle Ages has its analogue in the invasion of Europe by syphilis at the

end of the fifteenth century, which broke out in the form of a widespread and malignant epidemic and overran a large part of Europe, and which, after maintaining an excessive virulence for several decades, gradually lost its epidemic character and assumed the milder type which it exhibits at the present day. The phenomenal outbreaks of syphilis in the character of an epidemic or endemic in Scotland during the seventeenth century, in Norway and Sweden, and in various parts of Europe during the eighteenth century, may also be mentioned as illustrating the variable virulence of this disease.

The epidemic violence of leprosy when introduced in a new country where the racial susceptibility and habits of living favor its spread, and which has been so strikingly seen in the Sandwich Islands, New Caledonia, and other modern centres of leprosy, is only an illustration of the special virulence and malignancy which any infectious disease assumes when transplanted into a favorable soil. Other illustrations of this are seen in the ravages of syphilis introduced into Hawaii by Captain Cook's men in 1779, of measles in 1849, and of smallpox in 1853, and the pestilential violence of smallpox in Iceland in 1707, which killed eighteen thousand persons. The epidemic of measles in 1846 destroyed not only a large proportion of the inhabitants of Iceland, but killed almost all the lepers. Numerous other examples might be cited to show that the inequalities and irregularities of contagion by no means particularize leprosy, but are exhibited by all infectious diseases.

Modes of Infection.

Although the pathogenic agent of leprosy has been identified, and its constant presence in the lesions it causes demonstrated beyond all possibility of doubt, there are many points connected with the modes of its entrance into the system and the conditions which favor its growth and propagation which are yet undetermined. It is very probable that the modes of leprous contagion are many. While we must recognize that the knowledge of the possible numerous and varied processes by which leprous contaminations take place possesses the highest interest and importance from a prophylactic point of view, yet it must be confessed that the precise manner in which the leprous virus is transferred from one individual to another is unknown.

The bacillus lepræ must be transmitted either directly or mediately from individual to individual. It has been suggested that it may run through a stage of intermediate life (spore condition) which

we are at present unable to detect, either on account of the minuteness of the spores or on account of the imperfection of our staining methods; which may be present in the soil, water, or food, but can get into them only from diseased tissues of the leper (Arning).

It is possible that the contagious activity of leprosy, like that of syphilis and other infectious diseases, may undergo certain modifications during the evolution of the disease and be inoculable only at certain periods.

Whether leprosy may be propagated by inoculative contact, through sexual intercourse, through the skin by accidental wounds and lesions of continuity; whether it may be conveyed by the process of vaccination, by bites or stings of flies, mosquitoes, and other insects; whether its virulent principle may attach to the soil, water, and food and be introduced as are the germs of cholera by imbibition, or by inhalation of the virus contained in the sputum, disseminated in the form of dust through the air, as in tuberculosis; or whether objects surrounding the leper upon which the virus has been accidently deposited may serve as a medium of transference from one person to another, are points concerning which there is great diversity of opinion. The absence of any definite primary lesion upon the outer surface of the body which marks the point of entrance of the virus into the system tends to still further complicate the difficulties in solving the pathogenic problem.

Sexual Intercourse.—Although I formerly attached considerable significance to this possible mode of contagion, I now believe it plays a very inappreciable rôle in conveying the germs of leprosy. The thousand and one intimacies which attach to the married relation afford abundant facilities for infection quite independent of sexual contact. It is quite conceivable, however, that if the sexual organs are the seat of leprous lesions, as is not infrequently the case in the tubercular form, the abrasions or solutions of continuity of the mucous membranes which often occur in coitus constitute favorable foramina contagiosa.

In some leprous countries this mode of contagion is generally accepted by the laity and also by many of the profession as the almost exclusive mode of propagating the disease, the belief being based upon the observation that if the husband or wife is leprous the healthy partner often becomes contaminated, and that healthy persons having illicit relations with lepers frequently contract the disease. This opinion is so universal and deeply rooted in the Sandwich Islands that accusations of immorality were brought against Father Damien, based solely on the ground that his disease could have been contracted only through illicit intercourse. Two of my patients from Honolulu

have assured me that their principal dread of having the real nature of their disease known was that it would carry to the minds of their friends a conviction of their immorality.

Kissing.—It is well known that kissing represents one of the most common modes of syphilitic contagion; it is very probable that leprous infection may take place in the same way. In tubercular cases, as is well known, the buccal cavity swarms with bacilli which are present not only in the leprous lesions, but also in the saliva, which is mixed with the secretions of these lesions. Any break in the continuity of the delicate epithelial covering of the lips would render inoculation possible.

It has been suggested that the custom which exists in Iceland of kissing all persons present when entering a room may be a fruitful source of contagion. Dr. Ehlers has seen lepers thus kissed by well persons. On account of this custom he is opposed to the isolation of lepers in their own homes, as practised in Norway.

The custom of salutation, which is common among the Hawaiians, of kissing and rubbing their noses together when they meet has been suggested as one of the means of spreading leprosy in the Sandwich Islands.

Wounds and Abrasions of the Integument.—It is a question whether the virulent principle of leprosy may find entrance to the organism through cracks, fissures, or abrasions in the integument. The fact that the first appearance of the leprous manifestations is commonly on the exposed parts, the face and extremities, and that in countries where the natives go barefoot the plantar ulcer is often the earliest lesion, lends support to this view. It is worthy of note that in countries where leprosy is endemic, the opinion generally prevails that the disease is often spread by accidental inoculation through contact of broken surfaces. Since the demonstration by Babes of the passage of lepra bacilli along the hair follicles and through the intact skin and that the skin of lepers in tubercular cases may be coated with bacilli coming through the hair follicles, the theory of inoculation by contact with a leper's body is quite plausible.

Nursing.—Since the milk in women suffering from tubercular leprosy contains the parasite, Babes has expressed his belief that leprosy may be conveyed in the process of suckling. He reports a case in which a lesion on the cheek was observed as the first evidence of the disease in a child nursed by a leprous woman. In certain leprous countries, especially in India, the opinion prevails that the germs of leprosy may be conveyed in the act of nursing. Sir Ronald Martin states that the dangers to Europeans of contracting leprosy in India arise chiefly through nursing and vaccination.

Other observers also speak of the probability of the infection having been conveyed in this way.

Leprosy Communicated by the Bite of a Leper.—If leprosy may be inoculated through the skin, the possibility of this mode of infection is evident. I find in my notes taken in Molokai the following:

John G——, on July 4th, 1877, was bitten by a leper in an advanced stage, who died of the disease in 1883. The bite was on the middle finger of the right hand and cut through nearly to the bone. The hand and forearm at once became swollen, and were lame and painful, with shooting pains, for about a week. The wound gradually healed and the arm became as usual. Some years later he noticed that the right hand assumed a bluish appearance occasionally. Later on the other hand became similarly affected. Soon afterwards a bluish spot appeared on the right hand, which still persists, although it has now become yellow. Early in 1885 he was declared to be a leper and sent to the leper settlement. He firmly believes from all the circumstances that the disease has its origin in him from the bite of a native leper.

Vaccination.—The question whether leprosy may be conveyed to a healthy person in the process of vaccination possesses at the present time rather a retrospective than an actual interest. In many leprous countries the methods and appliances of modern medicine are employed, and the use of humanized has been supplanted by that of bovine virus. In some countries, however, even at the present day, where bovine virus cannot readily be procured, and especially when a smallpox epidemic threatens, arm-to-arm vaccination is still practised. It must be admitted that if leprosy be inoculable, arm-to-arm vaccination in leprous countries constitutes a direct and most effective method of conveying the germs.

Even when bovine virus is used, if a number of individuals, one of whom may be leprous, are inoculated in succession, the possibility of conveying the germs from one person to another, by not thoroughly disinfecting the lancet after each vaccination, must be borne in mind.

The clinical evidence that vaccination may be the means of propagating leprosy rests upon the observation of individual cases in which, for example, a single member of a family has been vaccinated and afterwards develops leprosy while the other unvaccinated members escape, and upon the rapid spread of leprosy in certain countries after a general vaccination. Of course, it is to be remembered that in leprous countries there must exist many opportunities for infection in other ways that may escape observation, and the proof is rather presumptive than positive. It is also claimed that as children, who are commonly exempt from leprous manifestations, are usually employed as vaccinifers, the danger is reduced to a minimum. It

should not be forgotten, however, that children may have the disease in a latent or undeveloped form, and the question then arises whether the disease is inoculable in its latent stage or only in a subsequent period in the evolution of the disease.

The most noteworthy individual examples of presumed inoculation by vaccination are two cases reported by Professor Gardiner, of Glasgow, and two cases of Dr. Daubler, of Robben Island.

Professor Gardiner reports that Dr. J. C——, a resident of a British colony, vaccinated his own son with the virus taken from a child presumably healthy, but who afterwards developed leprosy; and from his own child he vaccinated the son of a Scotch ship captain trading between Scotland and the colony. By an extraordinary coincidence Professor Gardiner had occasion afterwards to see both children, the son of the medical man and the son of the ship captain, in Scotland, both being affected with tubercular leprosy. In both of these cases the proof of leprosy having been conveyed by vaccination is presumptive, as the child of the doctor may have acquired the disease independently of the vaccination. In the case of the other child, who visited the colony only temporarily, the chances of accidental contamination in other ways were much less, and the evidence in favor of vaccination was stronger.

The first of Dr. Daubler's cases was that of a woman who was quite healthy until vaccinated in 1885. She had never in her knowledge come in contact with leprosy. About a year after vaccination a large livid patch began to appear around the vaccination mark. A few months later a creeping sensation on both sides of the face was noticed, and soon afterwards the face began to swell, and she developed a tubercular condition of both sides of the face and ears, with loss of the eyebrows and other evidences of tubercular leprosy.

The other case was that of a girl fifteen years old, who was quite healthy until she was revaccinated in 1885. She had never seen any one with leprosy to her knowledge. The same local appearances followed on the arms as those described in the previous case, and they were followed later by maculæ of the cheeks and leprous tubercles on the forehead. Investigation showed that the person from whom the lymph was taken died of tubercular leprosy.

Dr. Hillis reports a case of a Portuguese, born in Demerara, aged twenty, the son of healthy parents, and his sister, aged eighteen, who were the subjects of tubercular leprosy. They had both been vaccinated with lymph obtained from a Portuguese family known to be affected with tubercular leprosy. They were the only members of the family vaccinated with this lymph. Three sisters and one brother were perfectly healthy.

Mr. B——, an intelligent resident of Maui, narrated to me the following case coming under his personal observation: A family on the island consisted of the father, mother, and five children. The older members of the family having been vaccinated previous to coming there, only the youngest child was vaccinated with humanized lymph. This child alone of the entire family became a leper.

In the Sandwich Islands the opinion generally prevails that leprosy may be inoculated in the process of vaccination. This opinion was based upon the observed fact that there was a notable increase in the number of cases of leprosy after a general vaccination immediately succeeding the smallpox epidemics of 1852, 1868, and 1872, and that numerous leprous centres developed in various parts of the islands where the disease had previously been unknown. In many places vaccination was performed by careless and unskilful persons. Humanized virus was used, and it is presumed that careful discrimination was not always made between lepers and healthy persons as vaccinifers.

Dr. Arning says: "There can be no doubt as regards the synchronousness of the diffusion of leprosy and the introduction of vaccination into the Hawaiian Islands. I am able to state, having excellent authority for so doing, though unfortunately no statistics, that a very remarkable accumulation of fresh leprosy cases took place in 1871 and 1872, at a place called Lahaina on the island of Maui. This happened about a year after a universal arm-to-arm vaccination which had been most carelessly performed. From fifty to sixty cases occurred suddenly in this locality, which up to this time had been comparatively free from the disease." Impey, medical superintendent of the leper settlement at Robben Island, said: "I wish to draw attention to one very serious matter in respect to the spread of leprosy. It is contagious and can be communicated from one person to another by inoculation. In South Africa the reprehensible practice of arm-to-arm vaccination is carried on to an enormous degree. Some means should be employed to stop the dangerous practice of vaccinating with humanized lymph," etc.

Arning has demonstrated the presence of bacilli in the crusts of vaccine pustules in tubercular lepers. Dr. A. Mitra, chief medical officer of Cashmir, says: "I have on three occasions searched for bacilli, and in one instance I found them in lymph from a vaccinated leper."

Dr. A. Brown, in a pamphlet on "Leprosy in its Contagio-syphilitic and Vaccinal Aspects," says: "The unanimity and persistency with which vaccination, in markedly leprous countries, is charged with propagating and disseminating the malady, the well-confirmed

coincidence of leprous centres with vaccination centres, and the discovery of the specific bacilli in those leprously vaccinated ought to satisfy all who are capable of reading evidence or of rational reflection that controversy on the questions must and will ere long be silenced."

Tebbs, in a recent work, endeavors to demonstrate that the remarkable recrudescence of leprosy in various countries at the present day is chiefly due to inoculation through the process of vaccination. While such a sweeping statement cannot be unqualifiedly accepted, it must be admitted that the author has collected a vast number of observations which give plausibility to his views. It is, of course, only in countries where humanized virus is employed that this possible danger exists, which emphasizes the necessity of controlling the source of the vaccine matter.

Inoculation by Insects.—The theory that certain diseases are conveyed by insects rests on a firm foundation. The investigations of Manson and Ross on the intimate relations existing between mosquitos and the dissemination of malaria have given a new interest to this question. Again, in many countries where leprosy is endemic there is a more or less general impression that the germs of the disease may be transported from the leper by flies and mosquitos and inoculated into healthy persons. Although the communicability of leprosy in this way has not been demonstrated, it is quite credible and worthy of scientific investigation.

It is interesting to note that the plague of mosquitos and the plague of leprosy appeared simultaneously in the Hawaiian Islands. Mosquitos which had previously been quite unknown there were imported, probably from China, towards the end of 1840 (Arning).

The same observer states that he has frequently examined bacteriospically mosquitos engorged with blood, found inside the mosquito netting of beds containing cases of severe cutaneous leprosy, without discovering traces of bacilli either in or upon them. Others have examined flies and mosquitos which came in contact with leprous patients and pustules on the bodies of lepers, but the results have always been negative until recently Alvarez claims to have discovered the presence of bacilli in mosquitos engorged with the blood of lepers.

That mosquitos and flies are common carriers of leprous contagion would seem improbable, since if this were the case, the transference of the disease from lepers to healthy persons, in countries where these pests abound, would be much more common.

Ashmead, in speaking of the agency of mosquitos in conveying the bacilli of leprosy, does not limit his theory to the idea that the virus is conveyed by the insect's haustellum. He thinks that eating

fish, such as carp, which are fed on the eggs of mosquitos, may be the cause.

Dr. Hutchinson, in reviewing this theory of the etiology of the disease, states "that leprosy prevails on the seaboard where neither mosquitos nor mosquito-eating fish are found." It is probable that there are many places where leprosy prevails and where mosquitos are unknown. If the poison were conveyed by insects, we should probably have some localities where every person, residents and visitors all alike, would suffer, just as there are places where no one escapes malaria.

Inhalation.—While this mode of infection rests upon presumptive rather than positive evidence, recent advances in our knowledge of leprosy would seem to indicate that it plays an active, if not the most prominent, part in the propagation of the disease. It is possible that the germs are contained in the expired air, when the aerial passages are the seat of leprous deposits, and are projected in the process of sneezing and coughing. Just as in the case of tuberculosis, the sputum of leprous patients, which has been shown to be loaded with bacilli, may, I believe, when scattered through the air with particles of dust, serve as a means of transporting the contagion.

It is to be observed that the theory of contagion through the respiratory passages was held by the ancients. It was forbidden to lepers in walking to go between the wind and those passing by, lest they should be contaminated by the leprous emanations. In the Middle Ages the leper "was especially prohibited from walking in narrow paths or from answering those who spoke to him in the roads and streets, unless in a whisper, lest they be annoyed by his pestilent breath and with the infectious odor which exhaled from his body."

Imbibition.—Liveing believes that leprosy may be propagated by the imbibition of the secretions of those affected, much in the same way, though not in the same degree, as typhoid fever and cholera are propagated; but as leprosy is developed slowly there is far greater difficulty in tracing it home to its true source.

Fish Theory.—The fact that leprosy occurs more frequently along maritime coasts, where the inhabitants employ fish as their main article of diet, led doubtless to the popular tradition that leprosy was caused by salted or rotten fish.

Mr. Jonathan Hutchinson, who is the strongest supporter of the fish hypothesis at the present day, thinks fish may cause leprosy in one of two ways—either there is direct introduction of bacilli into the stomach or some element of fish food rouses into activity the bacilli which exist in the tissues. The hypothesis that fish serves an intermediary host function for the bacilli is improbable from the fact

that the bacillus has never been found in fish caught in epidemic areas, although frequent examinations have been made. The fallacy of the fish theory is proved by the fact that leprosy occurs among people who have never tasted fish, either because it was not obtainable or because its use was forbidden by their caste or religion.

Dr. Tholozan, of Persia, states that while there is a great deal of leprosy in Kurdistan, there are no large rivers there, and he is sure that the inhabitants never eat any fish. In Teheran, where leprosy does not prevail to any extent, salt fish is the staple article of food.

A view of the fish hypothesis, differing radically from that of Hutchinson, is taken by Neve, who believes that the lepra bacillus may find conditions favorable to its germination among the considerable number of organisms generated by putrefying fish, hence serving as a culture medium as well as a means of transport. Almost every article of food has been in turn incriminated as the etiological factor, as salted meat, especially pork, vegetables, milk, etc. Forster has shown that various bacilli may retain their vitality in salt meat. Milk also is especially liable to different forms of infection.

The herdsmen of Cashmere never eat fish, but consume large quantities of milk (twelve pounds of curds in twenty-four hours). This milk, it is claimed, could easily serve as a transporting medium for the bacilli as well as salted meat or any kind of impure food or water.

Hicks and Blanc believe that the influence of diet is limited to preparing a defective and inflammatory condition of the intestine for the reception of the bacilli, and in the study of the transmission of leprosy it cannot be a question of the particular kind of food, but only if the characteristic bacillus is present. If food contains the bacilli, they must have been derived from the diseased tissues of the leper. I believe that the bacilli may be deposited on vegetables, fruits, and other articles of food handled by lepers and in this way carry the contagion. We can also understand that certain foods may so modify the constitution of the tissues that they afford a more suitable soil for the growth of the bacillus which has been introduced into them.

Mediate Infection.—It is probable that infection may take place by means of clothing or objects used by the leper or through the intermediary of food, drink, pipes, cups, or other objects upon which the virus may be deposited.

Many authorities believe in the probability of this mode of transferring the virus, and instances are cited which would seem to prove the probability of infection occurring in this way. The popular superstition of the danger of handling tools or other articles which have been used by lepers doubtless has some basis in fact.

The case reported by Hawtrey, of an Irishman who had never

been out of his native country except for a short voyage to England, and who contracted the disease by wearing the clothes or sleeping in the bed of his deceased leper brother, who had become a leper in India; the case of a patient who came into the Leper Hospital in Norway with a history of no leprosy in his family comprising twelve brothers and sisters, but who seven years previously had bought a coat which had belonged to a deceased leper and which he wore daily; and numerous others of like tenor scattered through literature would indicate that the disease may be conveyed in this manner.

The wearing of the boots or shoes of a leper, it is said, may be the means of conveying the contagion. In India leprosy is believed to be propagated by bathing in the reservoirs which have become polluted by lepers. Numerous cases are reported of infection of laundresses who washed the soiled linen or bedding of lepers and who were never brought into close personal contact with lepers, which is a fact worthy of note.

The recent unsuccessful attempts of the health authorities of Honolulu to stamp out the disease by the absolute segregation of every person found to be affected with leprosy is said to be largely due to the fact that the clothing and belongings of lepers who are transported to Molokai are utilized by the family and friends of the leper. Many of the government physicians have called attention to this possible source of danger in perpetuating the disease.

Le Blond says: "There should be rigid laws in reference to the distribution of the effects of lepers. A native has no scruple in wearing the cast-off coat of his exiled brother or sleeping in his unclean bed."

Lindley says: "There are many things which could be done that would go far to lessening the dangers of contagion. In almost all cases where lepers are sent away their effects, such as mats, clothing, etc., are given to grieving friends and relatives left behind. These, of course, are great sources of contagion."

Besnier believes that the leper can soil with his pathological excretions the ground, his garments, bedding, linen, dressings, and the walls, and that the dust of his room may be a source of leprous contamination.

In this connection it will be of great interest and value to give the most recent views of the leprologists of all countries, which were presented to the Berlin Leprosy Congress, upon the modes of the transmission of the bacillus lepræ.

Sticker makes the sweeping statement that in about ninety-six per cent. of all cases the primary focus of the disease is in the nasal chambers and that leprous contamination is from nose to nose.

Lassar suggests that since lupus is primarily developed on the lips and nose of children by picking or scratching these parts, leprosy may be communicated in the same way, and recommends that children in leprous countries should be taught to avoid this habit.

Arning does not believe that the primary manifestation is in all instances intranasal. In many cases he had carefully examined the nose and found nothing. He had seen in one case at least the primary lesion on the skin. In countries where people go barefoot there are more cases in which leprosy begins on the foot.

Geill believes that the leper contaminates the soil and that it is through the soil that healthy individuals are most often infected. He thinks that in order to transmit the virulent bacilli certain qualities of soil, not found everywhere, are essential.

In India and Tonquin, where the natives go barefoot, the disease appears first on the feet in more than fifty per cent. of the cases.

Hellat (Riga), while accepting the theory that the bacilli may be inhaled, thinks that there is no proof that the vital power of the nasal mucous membranes, which is efficacious enough to expel and destroy numerous other bacilli, is powerless against the lepra bacilli. He thinks that the skin may be the seat of entrance and refers to numerous cases in which leprosy has been transmitted by boots.

Ehlers believes that the initial lesion of leprosy varies according to the geographical latitude and conditions of life. In Iceland the first manifestations appear upon the face and hands. As is well known to be the case in syphilis, there is no place that may not be the point of entry for leprosy. In this country the respiratory passages are the first affected.

Babes says the most important question is, whether we can consider the first visible manifestation as the place of entrance of the infection. He indicates the possibility of infection through milk in which he has found bacilli, and cites a case of Kalindero in which a child nursed by a mother with mixed leprosy developed an isolated leproma on the cheek.

Petrini thinks it possible that the bacilli may be introduced into the organism by means of certain aliments, as we see many cases of leprosy in families where the food is in common.

Abrahams believes that the lepra bacilli may enter into the human system in as many ways as may those of tuberculosis.

Alvarez says that in Hawaii one may incriminate as a means of transmitting leprosy the common use of the pipe, which is passed from mouth to mouth in families.

Jeanselme refers to his investigations which would indicate the

nose as the principal point of entry, as well as the most virulent source of contagion.

Hallopeau opposes the view of infection through the nasal mucous membrane and also by sexual transmission. If invasion through the pituitary membrane was habitual or even possible by atmospheric dust, we cannot comprehend why our patients living for years in a medium charged with infected dust should remain unaffected. He is inclined to accept the hypothesis of infection through linen, clothing, stings of mosquitoes, etc.

Neisser thinks that the contagion may be received by respired air, and the infection of the skin, mucous membrane, and nerves follows extending from within outwards. The intestinal canal is also a possible way. There is no heredity, and what we looked upon as heredity is infection favored by family life.

Hansen entertains the same view as Neisser, though he refers to mediate transmission through clothing, linen, shoes, and the furnishings of the habitations of lepers.

Petersen relates a case in which the primary localization was in the nose. He detected the presence of a large ulcer on the left side of the septum the secretions from which were rich in bacilli.

In the official examination of twelve hundred cases reported to the Russian Government, the disease was first seen in the extremities in ninety-two per cent. of the cases of nerve leprosy. In one-half the cases of the tubercular form it was first seen on the face.

Petersen states also that Professor Munsch, some time ago, gave it as his opinion that in a certain number of cases leprosy commenced in the nose.

Doutrelepont is inclined to accept the view of the nasal origin of leprosy.

Kaposi denies that the frequent nasal ulcerations seen in lepers signify that the nose is the port of entry. In his opinion the skin is the most common place of entrance for the bacilli, but in the present state of our knowledge it is impossible to say where the initial lesion may be.

Besnier says the principal ways of projection and reception of the bacilli are the mucous surfaces—chiefly the nasal cavities, oculoconjunctival and buccal cavities, pharyngeal cavity, cutaneous surfaces, and perhaps the digestive tract.

It is evident from the very comprehensiveness of these views, including almost every possible mode or channel of entrance, that our knowledge on this matter is only conjectural. Accurate knowledge is expressed in precise rather than in vague, loose terms.

It will be perceived, however, from the above-quoted views that

most leprologists incline to the belief that infection in leprosy takes place through the mucous membranes of the upper air passages. This theory presupposes the aerial transmission of the bacilli, as it is difficult to conceive how inoculation of these surfaces could be effected by mediate contact with objects upon which the bacilli were accidentally deposited.

Several years ago, before the investigations of Jeanselme and Sticker, upon the results of which this belief is based, were undertaken, the writer expressed his personal views as follows:

"In the writer's opinion, most observers err in assuming that there is *one exclusive mode of infection* in leprosy. It is probable that, like the bacilli of anthrax, glanders, and tuberculosis, the mode of entrance of the parasite into the system is not unique, but multiple. We know that the bacillus of tuberculosis, which presents so many analogies with leprosy, may enter through the respiratory tract, the intestinal mucous membrane, or be inoculated through the skin. I believe that, similarly, the bacillus lepræ may be introduced through more than one channel of entrance. Direct inoculation through the skin, in any of the manifold ways which have been considered, plays in my opinion, a very unimportant rôle in the propagation of leprosy. In the vast majority of cases, I believe that the vehicles of the virus through which contagion is effected are the secretions of the nose and mouth, and that the port of entrance is the mucous membrane of the respiratory and intestinal tract, with secondary infection through the blood or lymphatic system."

My observation and study since the above was written have more than ever impressed me with the conviction of the widespread prevalence of infection through the upper air passages. If it be established by further investigations that the bacilli lepræ most frequently follow the aerial route in penetrating the organism, it may be assumed that they find in this locality the tissue soil most suitable for their reception and growth.

Conditions Influencing Infection.

Individual Predisposition.

From the fact that in countries where leprosy is endemic and the bacilli are abundant many are exposed but few are infected, it is evident that predisposition does not depend upon causes which, acting upon all alike, would reduce the entire population to the same degree of susceptibility, but upon conditions pertaining to the individual. The whole matter of individual susceptibility resolves itself

into a question of the capabilities of the body to restrict and limit the growth of the bacilli. That predisposition must exist as a condition of leprous infection is evident from the observed fact that certain individuals are absolutely immune. They escape the disease despite the most prolonged and intimate contact with lepers and constant exposure to every condition favorable to the communication of the germs. Their immunity evidently depends upon a lack of receptivity, or a greater capacity of resistance to the action of the pathogenic agent.

In such individuals, even though infection takes place, the resistance of the tissues to the inroads of the bacilli may be manifest in the further evolution of the malady, which is exceedingly slow and protracted. In certain cases the capacity of resistance is sufficient to dominate and destroy the pathogenic microbes. Abortive cases are occasionally seen in which there may have been indubitable signs of leprosy which after a time disappear definitively, and the persons remain ever afterwards free from any manifestation.

Individual predisposition, whether inherent or acquired, must be recognized as one of the most powerful factors in influencing infection. This predisposition may be constituted by a native weakness or debility, due to a certain type of conformation or peculiarity of tissue organization which renders the tissues of the individual more vulnerable and less capable of resisting infection. Those physiological peculiarities doubtless determine the type of the morbid process according as the cutaneous or nerve structures are more or less predisposed to the action of the bacilli. The preferential infection of the integument in the tubercular form and of the nerves in the anæsthetic form can be explained only on the ground of an existing proclivity in the tissues of the individual which for lack of a better term has been denominated idiosyncrasy.

But quite independent of this inherent organic predisposition there are certain accidental conditions of a general or local nature which create a pathological predisposition by lowering the resistance. All causes or conditions which impair the health or lower the vitality of the individual predispose to contagion. Excessive work, poor food, privation, misery, bad hygiene, nervous exhaustion, etc., must be placed in the category of conditions favoring infection. It is only upon the assumption that the capacity of resistance may be lowered by various causes that we can explain those cases in which immunity, though manifest for a long period, may finally be lost and the individual fall a victim—just as in tuberculosis an exemption prolonged for years does not guarantee an absolute permanent immunity.

In addition to the causes acting upon the general economy, certain

local conditions may influence infection by creating in certain tissues a *locus minoris resistentiæ* and thus permitting the entrance of the bacilli through this weakened part. Even after the bacilli come in contact with the tissues they probably lie latent, without pathogenic action, until excited into activity by some special cause.

The more our bacteriological knowledge advances the more we recognize the importance of pathological modifications in the organism as a necessary condition of the growth and multiplication of bacteria. There are many morbid germs which are susceptible of becoming pathogenic but manifest their virulence only under special circumstances. It is well known that many microbes of a common order, the streptococcus, the pneumococcus, the colon bacillus, etc., though capable of causing serious infections, may remain upon the cutaneous or mucous surfaces or in the air passages absolutely inert and innocuous, until they are provoked or excited into activity by some pathological change which creates for these microbes a "morbid opportunity."

The specific microbes, especially those of tuberculosis and leprosy, would seem to form no exception to this rule. It is probable that they lie latent upon the mucous surfaces of the air passages and await their opportunity until some localizing influence creates a special aptitude on the part of these tissues to conceive and develop their pathogenic action.

Prominent among the local conditions which influence this mode of infection I would place the inflammation of the upper air passages, known as a "cold" or a "catarrh," which so often precedes the development of other diseases.

In all countries where leprosy is endemic "a cold" followed or not by fever is among the first signs of ill health. In South Africa, according to Impey, "if you ask a leper how he contracted the disease, he will almost invariably reply that it was due to a cold. I am of opinion that cold is the exciting cause of leprosy. The bacillus lies inactive in the system until it is excited into action by the body being subjected to a severe cold." Again, in speaking of the symptoms of the tubercular form: "The first symptoms of this form of leprosy usually manifest themselves after a cold. The patient when heated has a cold bath, or he has been out in a snow storm, or subjected to some severe cold and becomes feverish. He thinks he is suffering from an ordinary catarrh or from an attack of simple fever."

In his personal observations of leprosy in Colombia, Garces says: "Most people attribute the origin of the malady to cold after exposure, allowing the sudden cooling of the body after profuse perspi-

ration, living in damp rooms, going from a lower to a higher altitude," etc.

The testimony of many observers in leprous countries in different quarters of the globe is to the effect that "a cold" is most frequently blamed by the patient as the starting-point of the disease. The catarrhal condition thus engendered may not only favor leprous infection by heightening the vulnerability of the mucous surfaces, thus permitting a ready penetration of the pathogenic agent, but the changes in the tissues caused by the inflammatory fluxion may create the biochemical conditions favorable to the germination of the bacilli.

Since writing the above, I have received a letter from Mr. J. Dutton, who has charge of the Home for Leper Boys in the Molokai settlement, in which he refers to the modes of communication of leprosy. For thirteen years he has been in intimate daily contact with lepers, and his opportunities for studying the disease in all its phases give his observations a special value. He says: "I cannot point to any initial lesion, many of the cases are advanced when I first see them." . . . "I shall say here, however, that if there is an initial lesion in my case, something in the skin seems to have that appearance. I have always thought, however, that inhalation has more to do with acquiring the disease than is generally supposed. The mucous surfaces are usually much affected in advanced cases, and also in—I should say—a decided majority of cases not yet old or far advanced. I have wondered if leprosy and catarrh do not find congenial conditions when they meet—a sort of affinity. The results in many cases—so much like catarrh—emanate from leprosy, but the ulcerations are extensive and rapid. I have also wondered if the bacilli are really the first invaders, if their busy duties do not consist at first in merely occupying tissues, previously made ready, in some way to us as yet mysterious and unexplainable."

Unhygienic Habits and Surroundings.—While the seed and the soil are the essential elements in the production of leprosy, it is obvious that they are both neutral until brought into conjunction. For the successful cultivation of leprosy, it is necessary that the seed be implanted in the soil. The intimate and sordid contact which comes from the unhygienic habits and surroundings of certain races or peoples would seem to constitute the most effective means of carrying out this condition. This view is supported by the observation that in all countries where leprosy has rapidly spread, dirty habits and promiscuity or communism in the matters of eating, drinking, and sleeping prevail. To take, for example, four important epidemic centres of leprosy within the past century:

The propagation of leprosy in Norway has been ascribed as largely due to the unhygienic habits of the people. According to Leloir: "The Norwegian peasant is very dirty. The greater number of the peasants have never taken a bath. They may sometimes wash (once a week) the face and hands, and the feet once a year, but the other parts of the body are not washed from the day of their birth to that of their death. Their clothing is never taken off even for the purposes of sleeping. It is generally made of wool. Their garments are never washed. Dirt is allowed to accumulate upon them, and when not too rotten, they are often transmitted from generation to generation. They live promiscuously gathered together in a small house. The cabin of the peasant is a hut made of firs with a wooden roof covered with earth, upon which a little turf is placed. The chimney is often nothing but a hole made in the roof, and the rain falls through it to the beaten earth which forms the flooring. Dung and filth are accumulated around the house amidst pools of dirty water. Often pigs, poultry, and other domestic animals live with the family. Almost always several persons sleep in the same bed, which is nothing but a kind of wooden chest upon which are thrown some sheep skins or goat skins which are scarcely ever washed. If a stranger comes he shares the bed. Everybody eats at the same table, from the same dish, often with a common spoon and drinks from the same vessel."

In addition the Norwegian peasants are weakened by poor food, damp, piercing cold, and the physical exertion necessary to gain a meagre subsistence, while skin disorders, due to the general prevalence of scabies among them, furnish an open entrance for the lepra bacilli and the agents of putrefaction as well. It cannot be considered surprising that leprosy rapidly spreads under such conditions, while these same lepers, transported to the United States and adopting the more civilized customs of living, with greater cleanliness, in separate newly built houses, which are not filthy nests of contagion, have not spread the disease.

Hansen attributes much importance to the habit of sleeping in the same bed with lepers in connection with the communication of the disease.

Turning now to another important centre, we find that while the natives of the Hawaiian Islands are more cleanly in their persons, the same promiscuity prevails in their habits of living. The habits of the natives of the Sandwich Islands have been thus described to me by Mr. Meyer, the superintendent of the leper settlement of Molokai: "Their modes of eating are so extremely careless that inoculation can readily take place through the mouth by means of the saliva

or otherwise. They pass their pipes from mouth to mouth, whether any of their number is a leper or not; they kiss and rub their noses together; they eat out of the same calabash with their fingers, and drink out of the same cup; in eating fish or meat it is not cut up, but one takes the meat in his hand, and, after taking a bite, passes it on. They drink *ava*, which is prepared by others chewing the root, and whether the chewer is a leper or not is not considered. Foreigners also become addicted to this habit of *ava* drinking, and it is remarkable that most of the foreigners who have become lepers were *ava* drinkers. Most of them have been mechanics, and the only cause to which they ascribe their disease is having worked with lepers and handled the same tools. The disease may have been communicated in some instances from food handled by lepers in an advanced stage."

In Madagascar, Dr. Davison, quoted by Hillis, says: "Probably the dirty habits so prevalent in half-civilized nations must tend to aggravate the disease; eating from a common dish with the fingers; the custom, very common in Madagascar, of interchanging garments, and of all lying huddled promiscuously together at night cannot fail to render it more inveterate, even in the way of originating it. It certainly deserves notice that, while the laws of Madagascar excluded leprous persons from society, the disease was kept within bounds: but after they were permitted to fall into disuse, it has spread to an almost incredible extent."

In New Caledonia, another hotbed of leprosy, the conditions of life among the aborigines are thus described by Dr. Le Grand: "Naked or almost naked, covered with mosquito stings and scratches, they lie sleeping in their smoky huts upon dirty mats. The rags which serve them as garments, their turbans, their handkerchiefs, their pipes—all is in common, and the scanty *garde robe* makes oftentimes the tour of the tribe. Place among them a leper, the secretions from whose ulcerations are diffused over the garments, the mats, and the soil, the result is that the first parts attacked are the parts most intimately brought into contact with objects or neighboring bodies in the different acts of common life. In addition, the leper in New Caledonia has the detestable habit of making deep ulcerations in his spots and tubercles with the aid of pieces of glass, treating them with caustic applications, etc. In addition their bodies are covered with a thousand insignificant hurts from insect bites and scratches, which serve as ports of sortie in diseased persons, and ports of entry in healthy persons."

Dr. Le Grand believes that leprous contagion is effected by inoculation, but that the leper is contagious only at an advanced stage, when he becomes a sort of "ambulant ulcer."

Climate.—From the extensive geographical distribution of leprosy it is evident that its development is independent of conditions of climate and soil. It extends from the tropics to the Arctic regions. It is found in damp malarial subtropical regions and in those of temperate non-malarial zones. It is distributed through the length and breadth of India. On this continent, it prevails in both marshy and mountainous regions, in the lowlands of Louisiana as well as on the elevated tablelands of Mexico.

While the widespread and diversified distribution of leprosy precludes the possibility of climate *per se* being invoked as a causal factor, it must be admitted that it may materially influence infection. As a rule a hot, moist climate favors the development of leprosy just as a cold, damp climate does. Leprous patients do better in equable temperate climates. It is probable that a propitious climate aids in the extinction of the disease by its favorable influence upon the general health as well as by its tendency to diminish bacillary virulence.

Reference has already been made to the observations that leprosy transplanted to this climate or to that of Central Europe does not take root and flourish, and each centre of infection, instead of spreading, dies out from the lack of conditions favorable to its development. So far as we can apprehend the nature of these inhibitory conditions, a major importance must be assigned to climate.

In the dry, cool climate of our Northwestern States, leprosy does not spread, but rather tends to die out from natural causes; on the other hand, the warm moist, semitropical climate of our Southern seaboard seems favorable to its development. Just as in the case of tuberculosis, with which leprosy presents so many analogies, climatic conditions seem to lessen or reduce its infective capacity to the point of extinction. In certain parts of this country, as, for example, in the elevated regions of the Colorado plateau, tuberculosis is but feebly contagious. In Colorado Springs, which is essentially a city of homes for consumptives, where the population of 25,000 is not transient, as in many health resorts, but permanent, carefully compiled statistics show that during twenty years there had been only ten deaths from non-imported consumption. Now the multitude of consumptives living there must have furnished tubercle bacilli in plentiful abundance for infection. It is evident that in certain climates it is more difficult for the germs of both tuberculosis and leprosy to maintain their virulence and to find a suitable soil in the body for their growth.

Race.—No race is immune to leprosy. We must recognize, however, that racial peculiarities may influence susceptibility to the disease and modify its mode of evolution.

Leprosy is decidedly more common among the dark than the white races. In the far East, the Mongolic races seem to exhibit a special susceptibility to the disease; it is much less common among the Malays. The negroid races of the Philippines, the Malay peninsula, and the tribal representatives of this race in Java are not affected to any great extent, while the Chinese (wherever they have emigrated) form the bulk of the lepers. The pure Indian races of South America show a marked immunity as compared with the African and mixed races. The same observation applies to the inhabitants of the Antilles. In the West Indies there is marked preponderance of leprosy in the negroes over all other races.

Hillis comments upon the remarkable immunity from leprosy enjoyed by the aboriginal tribes of British Guiana, whereas it is common among the Boviander or the offspring of the Indians with the black or colored natives of the colony. This immunity may be due to their open-air life, their habits of cleanliness, and their isolation. He instances as a remarkable fact that the Warroo tribe, which was the only native tribe that constantly associated with the negro lepers, alone became contaminated, and that leprosy prevails among their descendants to the present day, while no other Indian tribe has become affected.

The extraordinarily rapid increase and terrible mortality of leprosy among the natives of the Sandwich Islands must be ascribed partly to the habits, but largely to the racial qualities, of this people. They have a feeble vital tenacity; their capacity of resistance is small, and they succumb readily to diseases from which the average Anglo-Saxon easily recovers.

Age.—While leprosy attacks persons of all ages, from infancy up to fourscore, or even fourscore and ten, the greatest incidence of the disease seems to fall in the third decade, from twenty to thirty years. It would appear that tubercular leprosy attacks the patient at an earlier age than the anæsthetic form, or at least the first manifestations are several years earlier; Hillis says ten years.

Sex.—There is an undoubted predisposition to leprosy conferred by sex. In all leprous countries the number of males who suffer from leprosy is always in excess of that of females. This proportion varies somewhat in different countries. In Norway, among 7,302 cases there were 4,164 men, 3,183 women. In Iceland, about the same proportion—4 men to 3 women. In Bosnia and Herzegovina Neuman's statistics gives 116 men to 16 women. In Cape Colony Impey's statistics show 1,296 males to 475 females. In British Guiana the proportion is about 3 males to 1 female. In Hawaii the number of male lepers is about double that of the females.

This disproportion in the incidence of the disease in the two sexes may be due partly to occupation, the males being more exposed to vicissitudes of weather, and from their manual labor more liable to injuries resulting in broken surfaces and wounds. In Eastern countries the rooted aversion of the women to see foreign doctors and the strict seclusion in which women are habitually kept by the rule of Mohammedan tradition doubtless make the discrepancy appear greater than it really is. In Hong-Kong, for example, statistics show that of 125 lepers there were only 13 females, or 10.4 per cent.

SYMPTOMS AND COURSE.

While tubercular leprosy is not sufficiently regular in its evolution to admit of its division into distinct stages or periods, we may, for the convenience of clinical description, speak of (1) a period of invasion, (2) a period of erythematous eruption, (3) a period of tubercular eruption, and (4) a period of ulceration, succeeded by a final period in which the clinical symptoms constantly increase in intensity and severity owing to the continued degeneration of the tissues and the diminished vitality of the organism damaged by the multiplication of the bacilli and their toxins, as well as by the absorption of the products of suppuration.

It must be borne in mind, however, that in the ordinary evolution of tubercular leprosy the cutaneous manifestations do not develop in an order sufficiently regular or uniform to enable us to draw distinct lines of demarcation between these stages. There is no sharp chronological limitation of the erythematous eruption. This form of exanthem may and commonly does recur coincidently with the eruption of tubercles and may continue its outbreaks during the entire course of the disease. During the active neoplastic period many of the tubercles may become ulcerated or disappear by a process of resorption long before the ulcerative phase of the disease becomes definitely established.

Likewise in describing the course of anæsthetic leprosy we recognize (1) a period of invasion, (2) an eruptive stage, (3) an atrophic stage attended with tendinous retractions, deformities, and anæsthesia, and (4) an ulcerative stage with consecutive mutilations.

Strictly speaking, the macular lesions of this form are practically permanent and persistent during the entire course of the disease. Anæsthesia is also a more or less fixed feature and may coexist with hyperæsthesia. Ulcerations and deformities, while common and characteristic, are by no means invariable features.

It will thus be seen that any schematic arrangement is one of convenience rather than of scientific accuracy. It is intended only to outline the general course of the disease and indicate the more prominent phases which it successively exhibits in its ordinary evolution.

The manifestations of leprosy present the widest variations in character, morbid activity, and the intervals which separate their outbreaks. The explanation of the apparently capricious character of the leprous process which is especially marked in the earlier stages must be sought for in the tendency of the bacilli to multiply at irregular intervals, periods of activity alternating with periods of quiescence and repose.

It will be convenient to study the invasive period of tubercular and anæsthetic leprosy together, since the phenomena of this period present nothing absolutely characteristic of either form.

Period of Invasion or Incubation.

The term "invasion" is employed in this connection with a clear comprehension of the fact that there is not in leprosy, as in certain other infectious diseases, a rapid and general intoxication of the system, but that during the entire life term of the malady there may be repeated and progressive invasions by the bacilli and their toxins of structures previously exempt. The phenomena of this period present nothing absolutely characteristic; they are essentially transitory and uncertain, and in many cases they may be so slight as to pass unperceived by the patient.

Leloir has suggested that the invasion period of leprosy presents certain analogies with the period of the secondary incubation of syphilis or with the prodromal period of certain forms of tuberculosis.

The claim of recent investigators, that leprosy has an initial lesion, would, if demonstrated to be constantly present, indicate a closer analogy between the primary phases of leprosy and syphilis than has hitherto been suspected. This leads to the inquiry:

Has Leprosy an Initial Lesion? The fact that the first cutaneous manifestations of leprosy commonly occur upon exposed parts—the face, hands, or feet—in the form of erythematous spots has led to the opinion, still held by many observers, that these spots represent the initial lesion, from which, as infective centres, the germs are distributed.

Arning has reported an instance of what he regards as a primary localization of the virus in the skin. The patient came from a non-leprous part of the United States to Honolulu. Three months after

her arrival she noticed a small, red, slightly raised spot on the left forearm, which slowly enlarged and in a year became anæsthetic. Two years later a group of papules developed around it. Lepra bacilli were found abundantly in the tissues.

Kaposi reports a case of what he regarded as the initial lesion upon the finger of a patient in the form of a bulla, which the bearer thought was caused by the sting of an insect. Later the face became infiltrated with anæsthetic lepromes. Hillis says that "if leprosy may be introduced through the integument, the initial lesion must be an ill-defined erythematous spot, soon followed by other macules in the vicinity or any other part of the body." Blanc asserts that this sort of history was received from a number of his patients, and that in one case such a lesion came under his observation.

In the vast majority of cases, however, in which the date of infection can be fixed with approximative certainty within narrow limits, the erythematous spots do not appear for months or years later and during this time the presence of certain prodromal symptoms indicates clearly that systemic derangement is already in progress. Besides, the presence of these spots is not an absolutely constant feature which invariably precedes the development of tubercles or degenerative changes in the nerves. The leprous spots must be regarded not as a primary lesion from which autoinfection takes place, but rather as the evidence of an already accomplished infection of the system.

The writer's views upon this point were expressed several years ago as follows (Morrow's "System of Genito-Urinary Diseases, Syphilology, and Dermatology"): "There is, so far as we can determine, no *initial lesion* of the integument. It is probable that in the mucous surfaces of the upper air passages, the pituitary or pharyngeal membrane, or other ports of entrance of the virus there may be an initial patch which serves as an incubating medium for the bacilli before they become more generally diffused through the system. This view is quite in accordance with our knowledge of the modes of infection in glanders, tuberculosis, and other bacillary diseases. But there is no evidence whatever to show that leprosy has a primary lesion of the external parts which corresponds in any way to the initial lesion of syphilis."

These conclusions, at which I arrived several years ago and which were based upon my clinical studies of the disease, would seem to be confirmed by bacteriological proof. The recent bacteriological investigations of Sticker and of Jeanselme and Laurens, the results of which were submitted to the Berlin Leprosy Congress (1897), and to which reference is elsewhere made, would seem to substantiate my state-

ment that the lepra bacilli, in many cases at least, are first deposited upon the nasal mucous membrane, which constitutes a favorable culture ground for their multiplication and subsequent dissemination through the system.

Of the one hundred and fifty-three cases studied bacteriologically by Sticker, evidences of leprous changes in the nasal mucous membrane were found in all but thirteen. He maintains that these changes caused by the bacilli constitute the *initial lesion* of leprosy, which he thus describes: "It is an ulcer, rarely a tubercle, situated upon the nasal mucous membrane, usually the cartilaginous portion. It is usually simply erosive; it may be more or less penetrating and ultimately leads to necrosis of the osseous framework of the nose." The best evidence that this is the primary focus he finds in the peculiar distribution of the early lepromata of the face, which indicates dissemination of the parasite by the lymph channels. These nasal changes, he asserts, often precede by several years the first cutaneous nodules or the first nervous symptoms and may persist during the entire course of the disease as an active centre of autoinfection as well as of contagion.

Jeanselme and Laurens found leprous lesions of the nasal fossæ, the mouth, throat, and larynx in sixty per cent. of the twenty-six cases examined by them. They conclude that the bacilli first penetrate into the organism through an insignificant erosion of the pituitary membrane, and that the alterations of the nasal mucosa constitute the first exterior manifestation of leprosy. Thus is explained how the leprous chancre hidden in the anfractuosities of the nasal fossæ always passes unperceived.

These observers make the important reservation that this hypothesis, however plausible in certain cases, should not be generalized in all, since in certain subjects leprous coryza does not appear until the disease is fully developed. This view coincides with that expressed by myself (*l. c.*) that the nasal mucous membrane is not the sole port of entrance, as the mode of infection in leprosy is not unique but multiple.

Incubation.—Even admitting the existence of a leprous initial lesion in the nasal fossæ as more or less constant, we have no data, since the moment of contagious contact is always indeterminable, which would enable us to establish the period of its incubation or what, from its assumed analogies with syphilis, might be termed the *period of primary incubation*. For the recognition of leprosy the so-called leprous chancre is practically non-existent, since we are unable to identify the disease before the advent of certain symptoms which point to a systemic infection.

The incubation of leprosy is understood to embrace that period which elapses between the introduction of the bacilli into the system and the appearance of visible signs of the disease upon the cutaneous surface or the evidences of characteristic changes in the peripheral nerves. This period varies within wide limits and is often very protracted.

It is probable that, for a time at least, the bacilli remain dormant and inactive. No sign, local or constitutional, indicates that infection has taken place. We do not know what process of preparation may be taking place during this period of apparent quiescence. Whether there is a real sleep or hibernation of the germ, as is maintained by Besnier—a latent phase analogous to that of a seed which conserves for a time more or less prolonged its torpid life until the moment when its germinative conditions are realized—can only be conjectured. Certainly the subsequent reactions which show that the seed has germinated and become endowed with virulence and infective capacity may not be in evidence until months or years later. It would appear probable that if the tissue upon which they are first deposited is inapt for their propagation, they are carried to and fro in the lymphatic circulation until they find somewhere a favorable soil for their germination and growth. From this source of generation the bacilli are transplanted to other culture grounds, which in turn constitute fresh foci of infection until a more or less general infection takes place.

During this process of invasion of the system by the multiplication of bacilli and the creation of new centres of autoinfection there are usually certain constitutional reactions, to be described in connection with the prodromes, which mark a phase in the evolution of the disease and furnish clinical evidences that the implanted germs are active.

The *duration of the period of incubation* varies within wide limits and may be quite protracted. It has been variously estimated at from a few weeks or months to several years—three, five, twenty years or longer. In countries where leprosy is endemic and where there is more or less constant exposure to the chances of contagion it is impossible to determine this point.

Observations have been made in cases in which a leper has removed from an infected to a healthy district and has communicated the disease to persons previously exempt from any possible exposure. In these cases the period which elapses between the coming of the leper and the date of the first leprous manifestations in others has been taken as the basis of calculation. Obviously, however, conclusions founded upon such a basis are loose and unsatisfactory, since weeks

or months may elapse before there is a concurrence of conditions favorable to infection.

An estimate based upon the observation of persons without leprous antecedents who have been exposed for the first time in travelling or passing a limited time in a leprous country, and who have developed the disease after their return, may be accepted as approximately correct. But even here, unless they can fix definitely upon the time and circumstances of a known exposure, or the duration of their stay has been brief, it is evident that such calculation is open to error. Thus I have been consulted by a patient who lived eight years in South America without any known exposure and who showed no signs of the disease until shortly after his return to this country. Now in this case it is not possible to determine at what period of his stay he received the infection. It may have been soon after going there or immediately preceding his return. In another case under my observation a patient who had spent two weeks in the Sandwich Islands presented undoubted symptoms of leprosy within ten months after his return. Arning's case, in which leprosy developed within three months after the arrival of the patient in Hawaii from a non-leprous part of the United States, has already been referred to.

Bidenkap reports a case in which the incubation was of only a few weeks' duration. Impey (South Africa) says: "While bacilli may be in the system for years before producing signs, I know of a case in which symptoms of leprosy were produced within three months after their introduction. In the majority of cases it does not exceed two years."

As examples of prolonged incubation, Daniellsen and Boeck, Leloir, and others report cases in which the duration of this period varied from ten to twenty or even thirty years. In almost all these cases the patient had removed from a leprous district to a country where the disease was not endemic.

According to Besnier, one cannot accept the idea that persons who have emigrated from leprous countries and who have developed the first signs of the disease dozens of years later in non-leprous countries present a real incubation of such length. "This delay," he says, "can be due only to the conservation of the bacillus in an inert state in some neutral part of the organism. This period of silence corresponds not to a gradual germination of the pathogenic agent, but to a real sleep, a hibernation of the germ." "True incubation comprehends the time which elapses between the moment when the lepra bacillus reaches an opportune place, finds the exclusively human biochemical elements necessary to its multiplication, and setting it in action, and the moment when the first leprous manifestations occur."

This duration varies according to the anatomical place of its localization and the vital conditions of the invaded tissues, but it does not necessarily exceed an average of several months."

I am convinced from my observation of a number of patients who have consulted me that the period usually accorded by most text-book writers to the incubation of leprosy is much longer than it actually is. By careful questioning of many lepers who have contracted the disease abroad I have found that their initial symptoms, many of which they had paid no attention to or had almost forgotten, antedated by several months or even years the appearance of symptoms recognized as leprous.

It is probable that many cases recorded in literature as examples of prolonged incubation may have had for years symptoms undoubtedly leprous, but of so mild and equivocal a character that their true nature was misinterpreted and referred to rheumatism, malaria, or some other malady. Besides, it must be remembered that the initial symptoms of leprosy are so variable, uncharacteristic, and absolutely indefinite that they never would be ascribed to leprosy in any country where the disease was not endemic or there were not decided reasons for suspecting its presence.

Among the conditions which contribute to advance or materially retard the date of development of leprous symptoms are the state of the patient's health, climate, food, habits of living, etc., and, as in the case of other infectious diseases, the slower the action of the pathogenic agent the more likely is it to be affected by extraneous influences.

The duration of the period of incubation is not determined solely by the specific germ, but depends upon conditions of individual receptivity. The germination of the seed is especially subordinate to conditions of the soil. The resistance of the patient's tissues to the bacillary invasion is one of the principal factors in lengthening this period. Poverty, dirt, poor alimentation, and unhealthy surroundings have been the appurtenances of leprosy in all countries and in all ages. Where persons live in low, damp habitations with malarial surroundings and frequently exposed to cold and wet the bacillus is excited into activity and the incubation is shorter. All observation goes to show that the removal of a person from a leprous to a non-leprous country tends to retard the development of the disease.

Prodromes.

In the majority of cases there are certain prodromal symptoms more or less pronounced, but exceedingly variable in their character and order of development, which precede the outbreak of the eruptive phenomena. While they are not sufficiently characteristic to indicate with certainty the nature of the disease, they give evidence that some sort of systemic derangement is already in progress long before any outward signs furnish the necessary confirmation of the diagnosis. In the present state of our knowledge it is impossible to determine the pathological basis of these prodromal phenomena. We do not know whether they are due to the topical effects of the bacteria or to a more or less general intoxication by the chemical products or toxins of the microorganisms.

It is probable that the mode of onset of leprosy is analogous to that of tuberculosis, in which local or constitutional symptoms, such as hæmoptysis, laryngitis, or bronchitis, may be evident long before there is a general invasion of the pulmonary tissues by the bacilli.

The constitutional reaction does not necessarily imply that there is a general infection, but only that there is a disturbing cause at work in some part of the organism. In the case of anæsthetic leprosy, it would simplify our conception of the morbid process and at the same time be reconcilable with the clinical evidence to assume that the phenomena of this stage are the expression of a peripheral neuritis, due to the impression of the bacteria and their toxins upon these structures, and entirely independent of any central nervous trouble.

Febrile Symptoms.—Fever is a more or less constant feature of the tubercular form of leprosy and may be considered as the most important initial symptom. The types of leprous fever vary. In malarial regions it is commonly of the intermittent type. Many lepers date the beginning of their disease to an exposure to cold, followed by an attack of what they considered at the time malarial fever. It has been observed that this mode of origin is more apt to occur among persons who live in damp, swampy localities, and it is possible that their malarial environment exercises a predominant rôle in determining the febrile access. The febrile concomitants of the outbreaks of leprosy at a later stage are probably due to the invasion of new parts of the body by the bacilli and the toxic effect produced by their emanations.

In perhaps the majority of cases the fever is of the remittent type. The febrile access is more apt to come on during the afternoon or evening, attain its maximum, and be followed by a remission in the

morning and forenoon. While the fall of the fever may be attended with moderate sweating, it contrasts in this respect with the drenching perspiration so common and distressing a feature of tuberculosis.

Weakness and Prostration.—Coincident with the febrile paroxysms there oftentimes exists a very marked degree of prostration, which may continue after the febrile symptoms have passed. Patients complain of weakness, of an indisposition for exertion, and of an inclination to sleep.

Digestive Troubles.—Loss of appetite, nausea, difficult digestion, and other morbid stomachal conditions are among the earlier manifestations.

While anæmia is common as a result of the digestive disorders, the progressive emaciation which is so pronounced a feature of tuberculosis is not common in leprosy.

Epistaxis.—Among the local symptoms rhinitis, often attended with a sense of tickling, sneezing, coryza, and not infrequently with epistaxis, more fitly belongs to the prodromal period than to the later one to which it is usually assigned.

Leloir regarded the epistaxis of leprosy as similar in nature to the prodromal epistaxis of typhoid fever, incipient tuberculosis, and other infectious diseases. Later investigations would indicate that it is a specific rather than a symptomatic manifestation, the pathological basis of which is the existence of primary leprous foci in the nasal mucous membrane. Their presence would explain the precocity as well as the comparative constancy of the irritative symptoms. This mild epistaxis, which proceeds from congestion of the nasal mucosa, is not to be confounded with the epistaxis which results from ulceration of the pituitary membrane and other destructive changes manifest at a later period. Irritative symptoms of the nose are much more common in the tubercular form.

The prodromes of the anæsthetic form are much more variable in kind and degree and are distinguished by their more marked neurotic character, pointing to the active participation of the nervous system in their production.

From the relatively small number of bacilli in this form general systemic disturbance is not so pronounced as in the tubercular form. Disorders of sensation constitute the most constant and characteristic feature of the prodromal period of anæsthetic leprosy.

Formication and pruritus, tingling and pricking, burning pains of the surface, which vary in degree of intensity, oftentimes of a severe character, are common in the invasive period. Some patients cannot keep still from the imperious desire to rub and scratch the limbs. At night the sensation is not entirely dulled by sleep, evi-

dences of which may be manifest in the morning in the shape of scratch marks unconsciously inflicted.

One of my patients described the sensation as that which attends the contact of air or water with a freshly abraded surface. On more than one occasion, as he informed me, he removed his shoe, feeling assured that he would find an abrasion of the surface. These sensations are not invariably present, but are more or less intermittent in character. They are exceedingly capricious in their seat, first in one locality, then in another.

These hyperæsthetic symptoms, which are doubtless due to irritation of the peripheral nerves, are not confined to the skin. Tenderness and pain of a lancinating, boring character may be felt in the deeper structures, usually in the extremities, in the toes or heel, about the ankle, often associated with a sense of stiffness and weight of the members.

Cephalalgia sometimes accompanied with vertigo has been noted among the precursory signs of anæsthetic leprosy. The cephalalgia varies in intensity and severity, and is usually more pronounced in the evening. The pain is more apt to be localized at the back and base of the brain, and may be quite persistent.

Various algias and *rheumatoid pains*, especially in the lower limbs, may be present in the prodromal period.

Disorders of the sudoriparous and sebaceous glands, although much more pronounced later in the evolution of the disease, may nevertheless be manifest in the prodromal stage. The first evidence of irregularity is usually observed in the abnormal excitability of the sweat glands, which pour out their secretion spontaneously or under the influence of light exercise, which normally would not provoke this secretion. This hyperidrosis does not depend upon anæmia or general weakness as in tuberculosis, but is due to vasomotor disturbance from peripheral nerve lesion and possibly, according to Leloir, to central complications.

All of the above-described symptoms vary in character and intensity. They may fail altogether or be so slight as to escape attention. As in syphilis, the prodromes are by no means constant and invariable. In many cases the patient does not feel any indication of disorder until after the appearance of the eruption. Their significance is rarely recognized or rightly interpreted until after unmistakable evidences of the disease have declared themselves. Even in countries where leprosy is endemic their occurrence, taken in connection with known exposure, would afford presumptive rather than positive proof of their true nature.

It will be more convenient to study separately the clinical features

of the two principal forms of leprosy, since the determination of the morbid process to the tegumentary system in the one form and to the nervous system in the other gives rise to such a diversity of manifestations that the clinical pictures presented by each are entirely distinct.

Tubercular Leprosy.

While the leprous process may affect various tissues and organs of the body, its most constant and characteristic manifestations are determined towards the skin and mucous membranes of the upper air passages. The clinical picture of this form is made up almost exclusively of the changes in these structures caused by the bacilli.

The eruptive elements consist of macular lesions, which may be simply erythematous or pigmented, infiltrations, diffuse, or circumscribed in the form of nodules, succeeded by the secondary changes of softening, ulceration, and crusting, or fibroid degeneration. The cutaneous manifestations are not, as a rule, continuously present in the early stage, but come out in successive crops. At first they are slight and transitory, but at a more advanced stage, they are permanent and impart to the disease a peculiar physiognomy which is pathognomonic (see Figs. 4 and 5). Their first appearance is important as marking definitely the début of the disease, and they often furnish the necessary confirmation of the diagnosis which was foreshadowed by the premonitory symptoms we have just been considering.

Period of Erythematous Eruption.

The first cutaneous manifestations occur in the form of erythematous spots or patches, which are sometimes described as *erythema leprosum* or leprous roseola. These spots exhibit a great variety of aspect in their size, shape, color, situation, and subsequent evolution. They are usually round or oval, sometimes irregular in outline, from the size of a lentil to that of a silver dollar or the palm of the hand.

The surface of the spots is as a rule flat and smooth, presenting a greasy, shining appearance without perceptible elevation or infiltration of the integument. All of the spots do not, however, correspond to this definition. Later they may be perceptibly elevated above the surrounding skin, with a slight degree of infiltration appreciable to the touch or even to the eye.

The color of the spots has been variously described as pinkish, reddish, vinous red, reddish-brown, coppery, mahogany, and of a sepia or iodine tint. These qualificatives indicate a wide diversity

in the color characteristics of the eruption as seen by different observers in different countries. The coloration varies according to the complexion and race of the individual, the age of the lesion, and certain extraneous conditions such as exposure to the sun, the wind, etc.

In the white race they are of a pinkish or crimson color, with a redness like that of ordinary erythema which deepens into a dusky red or a purplish hue. In brown and dark races the color is first a mahogany or brownish-red, assuming later a dark or even black coloration. In both races the color is apt to be more livid in dependent parts of the body, as on the legs and feet.

While the eruption may have a general distribution it has certain points of predilection. Most commonly it appears first upon the exposed parts, the dorsum of the feet, about the ankles, the backs of the hands and wrists, upon the forehead, cheeks, and ears. It may appear upon the buttocks, thighs, chest, and other portions of the body, but rarely upon the palms of the hands and soles of the feet. There is a certain degree of symmetry observed in its distribution.

The spots may increase in size, apparently like the spread of a drop of oil on a sheet of paper. The earlier spots are usually transitory, disappearing without leaving a trace or only a slight grayish pigmentation. In other cases they may require weeks or months for their involution. The color is at first usually more pronounced in the centre, fading towards the circumference; in other cases their contours are sharply defined. After a while the redness in the centre subsides, giving place to a brownish stain or only a slight pigmentation. Leloir has observed an ecchymotic tint similar to that seen after the disappearance of certain papular erythemas.

The spots are exceedingly variable in aspect, like that of erythema solare, chloasma, and various other pigmentations of the skin, and they have little diagnostic significance. Occasionally spots may appear in the form of a diffuse, somewhat erythematous blush or reddish tinge, and disappear promptly or in a few days without leaving a trace.

Garces, in describing the peculiarities of leprosy in Colombia, says that in that country "the initial exanthem of leprosy is almost always of the urticarial type. Most people attribute the origin of the malady to cold after exposure, allowing the sudden cooling of the body after perspiration, and living in damp rooms. These accidents are followed by the wheals of urticaria which are the starting-point of leprosy."

The outbreak of the erythema is frequently preceded or accompanied by evidences of constitutional disturbance, such as chills and fever, a general feeling of lassitude, malaise, etc. Local sensations of

pricking or itching may precede or attend the eruption or subjective sensations may be entirely absent. Some have described the sensation as of "ants walking over and stinging the face" (Hillis). The patches may develop insidiously, without the knowledge of the patient and unaccompanied by any local phenomena, and are then discovered by chance.

The spots are, as a rule, not permanent, but they may appear and disappear a number of times before the establishment of the characteristic tubercular changes without leaving any trace of their previous existence. The earlier eruptions are essentially erythematous, the coloration is affected by temperature changes and disappears temporarily on pressure. Later the patches are more pigmented, they pale on pressure, but the coloration is not entirely effaced.

Leloir divides the lesions of this stage into two principal groups, the *hyperæmic spots* and the *pigmented spots;* in the latter the pigmentation is secondary to the hyperæmia. This division appears to introduce an unnecessary refinement of distinction, as the pigmentation represents an evolutionary change which, as in the case of other lesions of the erythematous type, may be absent or present according to the duration and intensity of the capillary congestion.

With each congestive attack the new macules become larger in extent and more prominent than those of the first eruption. Gradually the pigmentation deepens into a brownish-red or bluish-red color, the skin becomes thickened, slightly raised, uneven, and, finally, the seat of tubercular infiltration.

As a rule, the spots are not anæsthetic; certainly there is no loss of sensibility at all comparable to what characterizes the spots of anæsthetic leprosy. Exceptionally there may be a very appreciable loss of sensation in patches which have become thickened and which have existed for a long time. Disassociation of the different modes of sensation is rarely observed. While the patches, as a rule, are rarely universal, there is often to be observed a marked change in the coloration and texture of the entire skin. In white races it may become dry and yellowish or bronzed—a tint which has been compared by Rayer to the skin of the mulatto.

During months and years the disease may remain practically stationary, the clinical picture being diversified at times by the disappearance of old spots and the appearance of new ones, and by their gradual transformation into the bluish-red infiltrated patches, which remain more or less permanent.

Period of Eruption of Tubercles.

After a time the pigmented patches, instead of undergoing involution, remain persistent, the skin becomes slighty thickened and swollen and the seat of tubercular infiltrations, which appear in the form of small pea-sized or larger nodules, which may remain stationary or rapidly enlarge. The tubercles may, however, develop upon new surfaces which have not been the site of preceding pigment changes. Exceptionally they may develop coincidently with the first erythematous eruption, constituting the precocious tubercular stage.

Fig. 2.

The eruption of tubercles is almost always preceded by febrile symptoms and other evidences of constitutional disturbance, with more or less hyperæmia and œdema of the pigmented patches. At a more advanced stage the tubercular outbreak may be attended by no appreciable rise of temperature.

The tubercles exhibit great diversity of aspect in form, volume, consistence, coloration, situation, and mode of evolution. They may be dermic or hypodermic in their situation. They usually appear in the form of small nodules, the size of a shot or a pea, and they may attain the size of a cherry, hazelnut, or pigeon's egg, or they may form large tubercular masses from the fusion of contiguous tubercles.

The coloration of the tubercles varies in different races. Ordinarily they are of the same color as the pigmented skin upon which they develop. In dark races they are pinkish, brownish-red, some presenting a mahogany tint or hue like that of an iodine stain. In white races they are pale or yellowish upon their first appearance, or they

may on growing older show a reddish-brown or bluish-red color, depending upon the region of the skin upon which they develop. On the extremities they are darker and more elevated than on the trunk.

In consistence the tubercle is at first comparatively soft and elastic, later it grows firmer and harder. The lesions are softer upon the trunk than upon the face and extremities. The surface is smooth as if oiled, and sometimes the tense epidermis breaks at the summit and there may be a branny or psoriasiform desquamation. They are at first painful on pressure, but later they become indolent and absolutely insensitive, probably because of pressure upon and degeneration of the compressed nerves.

The seats of predilection for the tubercles are the facial mask, the forehead, especially the supraorbital region, the cheeks, chin, nose, and lips, the lobes of the ears, the dorsal surfaces of the hands and feet, the ankles, forearms, and wrists, the outer aspect of the thighs, and the buttocks. The primary eruption almost invariably appears upon the forehead or cheek, the anterior aspect of the forearms or the outside of the thigh; Impey says in his experience the first tubercle is commonly seen at the inner border of the supraorbital ridge. They may develop upon any portion of the body except the hairy scalp, which is almost always exempt. They are rarely seen over the elbow- or knee-joints or upon the palms and soles, in which situation they are flattened rather than prominent. As a rule they are flatter on the trunk from pressure of the clothing. They may appear upon the genital parts, the scrotum, prepuce, around the anus or vagina, and exceptionally upon the glans penis.

Most authorities affirm that the tubercles never appear upon the glans penis. I have, however, a photograph of a Chinaman, whom I examined in San Francisco, which shows characteristic tubercles on the glans (Fig. 2).

In the earlier stage the tubercles are small, resembling the papules of syphilis, the tubercles of lupus vulgaris, of acne indurata, or of sycosis. The remarkable resemblance of the case illustrated in Fig. 3 to syphilis will be noted at a glance.

The boy, H—— A——, a native of Key West, Florida, is 14 years old; he has two sisters and a brother, all healthy; the mother and father, natives of the West Indies, both enjoy good health; one uncle has been a sufferer from a chronic skin affection for a number of years, said to be an eczema. Four years ago he had an attack of measles. Upon regaining his health, it was observed that he had a "rash," which did not fade, as was anticipated the skin trouble would. His general health, however, seemed good, but during the hot weather his skin would assume a peculiar hue, and in places small elevations would appear, all fading when a cool day came. From what I have

been able to glean, the boy had been most thoroughly treated for syphilis; he had been to school, and led his usual life until the fall of 1893, when he was sent to New York for advice as to the nature of his ailment. At the time I first saw him his condition was about as

FIG. 3.—Tubercular Leprosy (Early Stage).

follows: Skin sallow, tongue coated; pulse not so full and strong as one would expect to find in a boy of his age—accounted for when his heart was listened to, as that organ was weak, but no murmurs could be found. His appetite was poor, meat being sought for and vegetables avoided by him. He could not stand any fatigue, being unable to walk any distance or perform any laborious tasks. The tubercles, more prominent on the face than elsewhere, were also present on his extremities. His body was free from these neoplasms, but there were

areas which seemed to have lost the pigmentation, or the pigment was increased in some places and faded in others. No anæsthetic areas could be found. In his mouth, extending from midway of the hard palate to well on the soft part of the palate, was an ulceration with elevated borders. It was probably one and a half inches in length by one-half to three-quarters of an inch wide. He complained of no pain or inconvenience from this lesion, which improved greatly after he was placed upon nux vomica. An ulcerated condition existed on his right foot, just back of the great toe; also a spot on the inner side of each thigh. The ulceration on the foot healed kindly, but when the boy was last seen the two other ulcers were far from healing.

The boy was taken to the Hospital for Contagious Disease, where he remained until his death in January, 1898. I am indebted to Dr. J. M. Winfield, of Brooklyn, for further notes of the case.

The tubercular areas (face, neck, ears, arm, hands, legs, and feet) gradually became more pronounced, and the ulcerations were deep. Occasionally the skin would clear up, and the boy gain strength; he grew very tall, and was exceedingly sensitive to observation. His throat symptoms, which were present from the start, gradually grew worse, and at times great difficulty was experienced in swallowing. Once or twice the swelling of the glottis seriously interfered with respiration. This condition of affairs continued, each day the patient growing more and more anæmic and emaciated until he was finally obliged to keep his bed. His death occurred from suffocation.

The pharynx, epiglottis, and trachea were found to be thickened and ulcerated. There were never any sensory disturbances or patches of anæsthesia.

As the tubercles grow older, or as they develop at a later stage, they are larger and more voluminous and exhibit a more pronounced coloration. Sometimes they appear as small firm nodules closely set together, the spaces between them being accentuated as furrows. This massing of the tubercles is especially seen about the supraorbital ridges, and upon the extensor surfaces of the arms and legs. The tubercles in this location, while they may be closely aggregated, are usually well defined and sharply distinct from each other.

Instead of being isolated, the nodules may become confluent and appear in the form of large plaques of thickened skin of variable size and extent (*lepromes en nappe*). These plaques are somewhat elevated, bluish, livid, or violaceous in color or even brownish or black (*morphœa nigra* of the ancient writers). In consistence they are firm, and Leloir compares the plaque to a piece of cardboard mortised in the skin. In other cases, the infiltration may become thick and denser, like a hard œdema of the skin and subcutaneous tissues; Bazin has termed this condition *leprous scleroderma*.

The surface of the plaque is usually mammillated, rough, and un-

even, and sometimes the seat of epidermic desquamation. The plaques vary in size from that of the palm to extensive infiltrations covering the entire surface of the limb. They are usually sharply demarcated; at other times they blend almost insensibly with the sound skin. They may exist for years without undergoing marked changes. In one case, which I had under observation for several years, the plaques on the extensor surfaces of the arms and thighs remained unchanged. Campana has shown that there is usually an elevation of temperature, from one to two degrees, to be observed over these plaques, which is sometimes succeeded by a subnormal temperature.

The disease extends by the invasion of new areas of previously unaffected skin and the development of new tubercles or plaques in the neighborhood of existing tubercles. In many cases there is a gradual increase in the sizo or volume of the tubercles. In other cases there are repeated congestive attacks which are synchronous with the multiplication of the bacilli, and, since the growth of the bacilli does not take place at a uniform rate, these attacks or exacerbations occur at irregular intervals, often accompanied by fever and general symptoms. They commonly coincide with or may be consecutive to softening and resorption of numbers of the tubercles.

These exacerbations may simulate an attack of erysipelas or of erythema nodosum, and, according to Leloir, they are due to resorption of leprous virus by the lymphatics and its extension along these channels. Evidence of this, he claims, may be found in the fact that there are often observed painful swellings of the neighboring lymphatic ganglia and ribbon-like prolongations of lymphangitis. Not infrequently there are rheumatoid pains and painful swellings in the joints in connection with these exacerbations.

At this period the skin of the face becomes tumefied with a shiny, glazed, discolored appearance, the backs of the hands and feet are often puffy and swollen with a diffuse infiltration, especially marked over the dorsal surface of the first and second phalanges, giving the fingers a fusiform appearance. The dorsal surfaces of the feet may be similarly affected. Frequently the skin about the ankle and leg becomes thickened and indurated and the seat of a hard, œdematous swelling, which may be covered with large imbricated scales with papillomatous proliferations. This pachydermatous condition presents a striking resemblance to that of elephantiasis arabum.

It is to be remarked that the process of ulceration in old tubercles occurs coincidentally with the development of new ones.

Daniellsen and Boeck have observed that congestive attacks which precede or accompany the appearance of new tubercles are often syn-

chronous with the breaking down and resorption of old ones. This process is usually accompanied by fever and general phenomena of systemic disturbance which disappear spontaneously.

The new tubercles remain stationary or develop until, with a new congestive attack, they undergo the same evolutionary changes. According to Leloir the skin which surrounds the tubercles becomes red and there develop localized tumefactions, resembling those of erythema nodosum, which are gradually transformed into new leprous tubercles, at the same time augmenting the volume of the preëxisting tubercles around which they are developed.

FIG. 4.—Typical Facies of Tubercular Leprosy. (From Morrow's "System of Genito-Urinary Diseases, Syphilology, and Dermatology.")

In countries where leprosy is endemic, it has been observed that the tubercles become larger and more marked for three or four years, when they begin to break down and ulcerate.

The evolution of the tubercles is not sufficiently regular to admit of chronological classification. Their most marked and characteristic development occurs upon the face, and gives that peculiar aspect to the individual which has been denominated *leontiasis*, and which is pathognomonic of the disease. (See Figs. 4 and 5.)

In the advanced stage the integument of the face becomes infiltrated with tubercular nodules or masses which exaggerate the natural lines or furrows of the skin. The supraorbital regions are studded with the tubercles, most marked towards the internal border, and form protuberant masses separated by vertical furrows, which intersect the horizontal furrows, forming lobulated masses. The cheeks, especially

over the malar prominences, are enormously tumefied and uneven with tubercles. The lips are swollen and everted, the alæ of the nose thickened and broadened, the chin is enlarged and covered with bossy protuberances, giving it a square appearance, the lobes of the ears are enlarged, hanging down in flabby pendulous masses. These, with the loss of the eyebrows and lashes, the conjunctival and corneal lesions, are elements in a picture of hideous deformity which once seen can always be recognized as pathognomonic.

Fig. 5.—Typical Facies of Tubercular Leprosy. (From Morrow's "System of Genito-Urinary Diseases, Syphilology, and Dermatology.")

The course of the tubercles and diffuse infiltration may remain stationary and practically no change take place, except in size, for months or years, the surface desquamating and the color changing into a coppery, dark brown, or livid tint.

The tubercles may undergo gradual resorption or become transformed by a process of fibrous induration into small masses, which persist indefinitely without further change, or they may take on a keloidal character.

The disappearance of one group is succeeded by another in the same or new regions at variable intervals.

Lymphatic Ganglia.—Implication of the lymphatic ganglia may begin at an early stage of leprosy. Swelling of the glands is most pronounced in the inguinal region. Usually the swelling increases with each congestive attack, and the glands may attain the volume of a nut or even a goose egg. The cervical and axillary ganglia may also attain to large a size. The swellings of the submaxillary and sublingual glands may be so pronounced as to impede the movements of

the jaws and even interfere with the process of deglutition. All of the glands of the body accessible to the touch may be found enlarged, the popliteal, epitrochlear, etc. It is probable that there is coincident enlargement of the mesenteric glands, as has been demonstrated by autopsy in many cases. There is a hyperplasia of the connective tissue.

The glands rarely soften and ulcerate, but in the final stage there may be found fistulous tracts communicating with the ganglia from which a large quantity of thick matter escapes. Leloir believes that the lymphatic ganglia are veritable sources of the leprous virus, constituting centres of autoinfection, and that their condition is always in direct relation to the course of the disease. In the early stages they are but slightly swollen, but later, with the multiplication and accumulation of the bacilli, they become large and painful.

During this entire period there are to be observed certain changes in the glandular portions and appendages of the skin, and sensory disorders more or less pronounced.

The *sebaceous* and *sweat glands* are disturbed in their function at an early period of the disease. The alterations of the glandular apparatus are often noticeable during the erythematous stage, but become more pronounced with the progress of the disease. There is generally an increase in their functional activity, expressed by hypersecretion, which is followed by diminution or arrest, which may be general or localized in certain areas.

The exaggeration in the function of the sebaceous glands in the early stage gives the skin a characteristic shiny appearance, as if it had been rubbed with oil. Later the sweat disappears from the affected regions and sometimes is suppressed over the entire body, and the skin becomes dry and harsh from the disappearance of the glandular secretions.

Hair Follicles.—The leprous process usually affects the pilous elements of the skin in the most destructive manner. The alopecia is first manifest in the fragility, thinning, and falling of the hair, and later in complete loss of the hair in certain regions. The falling out of the hair is, as a rule, confined to the localities affected by the eruption and is absent over the spots and present in the intervals between them. Usually the first to suffer are the eyebrows, the loss of which constitutes one of the most characteristic features of tubercular leprosy, and is valuable from a diagnostic point of view. The alopecia also affects the beard, the nostrils, and other pilous portions of the body which are the seats of tubercular infiltrations. Upon the face the conservation of the hairs in the intervals between the leprous infiltrations give the beard a sort of tufted appearance (Fig. 4).

The hairy scalp enjoys a surprising immunity from the encroachments of the bacilli. It is not uncommon to see a leper with a fine growth of hair on the head, while the hair has almost disappeared from the rest of the body. On the general surface of the body the hairs suffer from a pronounced inanition before gradually disappearing, becoming dried, atrophic, and easily broken.

The development of leprosy before puberty exercises an inhibitory effect upon the growth of the hair over the entire surface of the body. There is commonly observed an arrest of development of the hair in the axillary, pubic, and facial regions; the eyebrows and body hair fall out subsequently, leaving the body entirely glabrous.

Sensory Disorders.—The disorders of sensibility are not constant or characteristic features of tubercular leprosy. In many cases even of extensive distribution of tubercular lesions sensation may be preserved in complete integrity. Certain of the lesions may be at first hyperæsthetic succeeded by anæsthesia, and in rare cases there may be dissociation of the modes of sensibility, as in anæsthetic leprosy.

It is probable that the anæsthesia of the tubercles and surrounding skin is caused by pressure upon the terminal filaments of the cutaneous nerves, which pass into the tubercle, and the cuticle becomes anæsthetic from paralysis. It has been observed that sensibility may return in parts that have been anæsthetic, which would indicate that the phenomenon is caused by compression rather than by degeneration or destruction of the peripheral nerves. In general it may be said that the older the lesion the more accentuated the loss of sensation.

Leprosy of the Mucous Membranes.

The changes in the mucous membranes caused by leprosy have always been regarded as constituting one of the most characteristic features of the disease, but the chronological order in which these changes take place has not until recently been recognized. The general consensus of opinion has been that morbid alterations in the mucosa never occur before the skin is affected; while most writers assign the date of their development to a period long subsequent to the appearance of the cutaneous manifestations.

In an article on "Leprosy," written several years ago (*loc. cit.*) the present writer expressed his views as follows: "Contrary to what is usually taught, I believe that the first manifestations of leprosy are, in the majority of cases, determined toward the mucous membranes of the pharynx and upper air passages. Few of our modern authorities seem to recognize the precocity of these manifestations, although Hillis remarks that in tubercular leprosy the first

throat manifestations occur during the febrile attack. According to my observation, alteration of the voice, betrayed by a slightly husky or rough phonation, rhinitis, with an abnormally free nasal secretion, sometimes epistaxis, and an increase in the salivary secretions are among the earliest signs of leprosy." "At a more advanced stage, when there are leprous deposits in the mucous surfaces with involvement of the cartilages and bones, the characteristic, harsh, raucous voice and the difficult, sniffling respiration from obstruction of the nostrils are almost invariable concomitants."

It has usually been asserted that in anæsthetic leprosy the mucous membranes of the upper air passages are not implicated. In a number of cases collected by Gluck, he found the mucosa of the lips affected four times, the tongue twice, palate and throat three times, larynx four times, and nose fifteen times. Undoubtedly there are many cases of anæsthetic leprosy in which symptomatic manifestations are present when the existence of specific lesions in this locality cannot be demonstrated.

A patient in the early stage of anæsthetic leprosy, now under my observation, cannot go from a warm room into the cold air without liability to a copious nasal secretion compelling her to use a handkerchief almost continually. In this case there are no visible leprous changes in the nose, and the phenomenon is probably due to the action of the bacilli upon the vasomotor nerves of the pituitary membrane robbing it of their protecting power, so that it responds to the action of the cold air by an abnormal secretion. The increased salivary secretion may be caused by reflex irritation of the salivary glands. Jeanselme and Laurens claim that leprous coryza is not necessarily dependent upon previous infiltration, and that the coryza becomes attenuated or disappears spontaneously when the leprosy tends to become anæsthetic.

According to Hillis, coincidently with the appearance of tubercles on the cutaneous surface the mucous membranes of the mouth, the pillars of the fauces, the uvula, and the tongue may become studded with pinhead-sized papules. It will be more convenient to study the mucous-membrane manifestations of the different regions of the upper air and food passages separately.

The Nasal Mucous Membranes.—First in point of frequency, as well as in importance, are the changes in the nasal mucous membranes caused by leprosy. The investigations of Sticker and of Jeanselme and Laurens, to which reference has been elsewhere made, throw considerable light upon the pathological alterations of the nasal mucosa. A unique importance has been given to leprosy of the mucous membrane by the demonstration of the precocity of its manifesta-

tion. These authorities state that leprous coryza, which may simulate ordinary coryza, constitutes the first exterior manifestation of the disease in a large proportion of all cases. In lepra nervosa it shows a tendency to disappear spontaneously. In the tubercular form, on the contrary, it undergoes exacerbations from time to time, and these coincide with the cutaneous efflorescences, the rhinitis being often caused by leprous infiltrations in the nasal mucous membrane.

Among the most important symptoms of the initial stage is epistaxis. This may have the same importance as a revealing sign of leprosy as the hæmoptysis which is premonitory of pulmonary tuberculosis. The epistaxis may be quite abundant and accompanied with congestive phenomena, vertigo, etc., in the initial stage, but later becomes reduced to the loss of a few drops of blood when the patient makes an effort to expel the crusts which obstruct the nostrils, and later ceases altogether. In all these cases there is a marked tendency to erosion and superficial ulceration of the pituitary membrane, which becomes covered with thick adherent crusts formed by the abundant mucous or sanguinolent secretion.

As the disease advances the ulcers, which are usually situated in the septum, become deeper and more extensive, and finally perforate the cartilaginous septum. This perforation may be circumscribed and of limited extent, circular or elliptical in form, readily permitting the introduction of a probe from one nostril into the other. More often the septum is destroyed in its totality with, or more frequently without, involvement of the bony framework of the nose. The nose becomes deformed, sunken, flattened out, the lobules almost touching the upper lip and separated from it only by a slight gutter. The destruction of the cartilaginous septum occurs very insidiously and without the knowledge of the patient. It would seem to take place by a process of interstitial absorption, since expulsion of cartilaginous sequestra has not been observed.

The rhinoscopic picture of the pathological alterations which explains the functional troubles and the mechanism of the production of the characteristic deformities of the nose is thus given by Jeanselme and Laurens:

"Immediately above the vestibule, the skin of which is almost always intact, the mucous membrane is red, turgid, and furrowed with tortuous and distended capillaries. This congestion attains its maximum at the anterior and inferior portion of the septum. At this point the mucous membrane is often covered with small brownish crusts—vestiges of recent hemorrhages or of erosions more or less extensive lined with mucopus. The slightest touch of the probe

over this hemorrhagic zone provokes a sanguinolent discharge. The mucous covering of the entire inferior segment of the septum is ordinarily quite thickened and its consistence sensibly diminished. Sometimes, also, the pituitary membrane which covers the inferior turbinated bones is infiltrated, soft, and depressible. In one of our patients the middle turbinated was voluminous, of a blanched color, and was covered with a multitude of small congested points, of an almost ecchymotic redness."

At a more advanced period the septum is easily depressed by the probe, the consistence of the cartilage is notably diminished, and perforation takes place. "When the perforation is recent the free border is thick, callous, and bleeds easily. When it has existed for some time, the mucous membrane is thinned, pale, and cicatricial. These two aspects may be observed in the same perforation, one portion of the circumference being already cicatrized, while the other is still in an ulcerous condition—one never finds the cartilage denuded. When the rhinitis disappears the membrane which covers the turbinated bones may undergo a certain degree of atrophy, resulting in a considerable gaping of the nasal cavities, and bringing into view quite a large surface of the posterior pharyngeal wall."

In addition to the changes caused by leprous rhinitis there is sometimes observed a deposit of leprous tubercles which may be distributed over the lower turbinate, the septum, the floor, or vestibule of the nares. They are of variable number, flattened, lenticular, firm to the touch, and contrast by their grayish-white or pinkish color with the deep red of the mucous membrane. Ordinarily isolated, they may become confluent and form a continuous opaline and mammellated *nappe*. The vibrissæ fall out at an early stage.

All authorities agree that notwithstanding the destructive characters of the nasal lesions the sense of odor persists intact with scarcely notable modifications.

Sensation is often notably diminished or entirely abolished over the affected portions. Thus it may be entirely lost in the membrane covering the septum—so that one may freely cauterize the region of the septum without provoking pain, while the skin of the vestibule of the nares is normally sensitive. In certain cases anæsthesia may be entirely independent of any eruptive manifestation.

The Mucous Membrane of the Mouth and Throat.—Three-fourths of all cases of tubercular leprosy show mouth and throat lesions; in the anæsthetic form the proportion is much smaller.

The mouth and mucosa of the lips are often affected. The leprous infiltration causes a general thickening, with a superficial production of nodules. These may excoriate or ulcerate, and healing

with scars results. The infiltration is accompanied by a tendency to form rhagades which are deep, painful, and bleed readily. Ulcers are especially prone to occur on the free border of the lips and in severe cases healing is followed by stenoses and entropion of the mouth.

Gums.—The gums are affected rarely and late. When they do not actively participate they are hard, pale, and smooth. When they are actively involved they are swollen and eroded on the edges; retraction follows.

Cheeks.—The mucosa of the cheeks is involved even more rarely than the gums. The appearance when not actively participating is pale red.

The Tongue.—Leprous lesions of the tongue may appear in the form of tubercles or opaline patches. The tubercles exhibit considerable differences in size; ordinarily they are miliary, lenticular, pea-sized. Sometimes they are quite voluminous, hard or soft, reddish or livid in color, and with a smooth or vegetating surface.

The most characteristic features of leprosy of the tongue are nodules seated usually in the middle of the dorsum. They are rarely found elsewhere than on the dorsal aspect. They are usually multiple and may be discrete or confluent. When they are discrete the tongue has an irregular lobulated surface, the nodules being separated by furrows. When confluent, the nodules have a tessellated formation. The fusion of the tubercles may form a mammillated plaque, with a grayish surface, as if cauterized with nitrate of silver. Unlike intranasal nodules they do not usually break down, and have been known to persist for years without change.

The number of nodules and degree of infiltration tend to increase until the tongue becomes enlarged, thickened, and clumsy, sometimes twice the normal size, and can be moved with difficulty, mastication becomes difficult and painful, while the furrows between the tubercles crack and fissure. When ulceration occurs the ulcers are superficial with slightly undermined edges and resemble ulcerated mucous patches; the resulting scars also resemble syphilitic plaques. The thickened grayish epithelium may come away in rags, leaving the subjacent parts a little red or pale. The lingual papillæ are prominent, and the follicles at the back of the tongue hypertrophied; the two branches of the lingual V may form a considerable elevation.

Sensibility is usually abolished more or less completely in the surfaces occupied by the leprous infiltrations. Deep cauterizations with a hot iron may occasion no sensation. The thermic sensibility may also be lost. The sense of taste is in the majority of cases preserved in more or less complete integrity. Only occasionally do we see pinhead to lentil-sized nodules.

Lesions of the mouth may be accompanied by salivation from reflex irritation of the salivary glands.

Palate and Uvula.—These tissues are often affected coincidently with the cutaneous eruption which follows an attack of fever. The palate is generally occupied by a sharply limited infiltration, slightly raised and covered with a bluish or grayish opaline or epithelial coating, which may be slightly eroded. At a later period the entire palatine arch may become covered with an eruption of grayish and flattened tubercles of the form and volume of a split pea. These nodules may spread over the uvula and the anterior pillars of the palate in quite a symmetrical manner. The infiltration may extend forward, involving the membrane covering the hard palate, and extend to the retrodental furrows situated behind the superior incisors, often leading to shedding of the teeth, especially the incisors. The uvula is usually elongated, thickened, and of a peculiar grayish-blue color. A tubercle may form at the tip of the uvula, giving a bulbous appearance, or one may form at its junction with the velum, causing œdema and hypertrophy. The whole picture of the palate and uvula is strikingly like moist, vegetating syphilides.

Sooner or later there is erosion or ulceration which, as a rule, rapidly cicatrizes. The anterior surface of the uvula is particularly prone to ulceration. The ulcers are usually as large as a lentil, and as they heal new ones may appear until the whole infiltration may be replaced by cicatricial tissue. As the ulcerated uvula heals it may be contracted towards the palate; or it may be fixed in one of various vicious positions from adhesions with the surrounding structures. The various resulting deformities may seriously interfere with normal deglutition—regurgitation of liquids through the nose is common. As cicatrization proceeds there is more and more shrinkage and the pressure appears to cause rarefaction and absorption of the palate bones. The results again strikingly resemble the destructive lesions of tertiary syphilis, although the pathogeny is quite different.

It is to be observed that exceptionally the mucous membrane of the palatine arch presents a remarkable pallor, and that this anæmic condition may be manifest over the entire extent of the buccal and pharyngeal mucous surfaces.

Fauces.—Both the palatine arches and the tonsils are commonly affected. The ulceration of the infiltrated faucial pillars is rather superficial, while that of the tonsils is deeper and leads almost to the effacement of these structures. The leprous ulcerations of the tonsil are often covered with a grayish diphtheroid coating and simulate closely syphilitic ulcers of these structures.

Pharynx.—The posterior wall of the pharynx often escapes, yet may be involved when structures like the nose and mouth escape. Leprous pharyngitis resembles leprous rhinitis; the membrane is oily, red, and shiny as if varnished. The nasal insufficiency which compels the patients to breathe almost exclusively through the mouth is probably the principal cause of this dry and parched condition of the mucous surfaces. There is an irregular deposit of small nodules which become eroded or ulcerated and heal with white superficial scars. On account of coincident anæsthesia, patients do not feel much pain unless there are deep rhagades or deep ulcers.

The Ear.—Leloir and others make mention of certain auditory troubles which occur in the course of leprosy. They are usually confined to noises and rumblings in the ears with decided dulness in the acuity of the sense of hearing. The condition of the alterations in the tonsil, with congestion and thickening of the membrane of the Eustachian tube with consequent obstruction, explain these auditory phenomena. There is often also some redness and congestion of the membrana tympani. The hearing may also be temporarily affected by the development of nodules in the external auditory canal, coincident with their appearance in the external parts of the ear.

The Larynx.—The epiglottis is the region of the larynx most frequently involved in leprosy. There is infiltration or hypertrophy of the submucous connective tissue and the epiglottis becomes thickened, tumefied, and stiff. The mucosa may remain smooth or be studded with small grayish nodules, and the usual ulceration and scarring may be present. Sometimes this covering becomes thickened and is transformed into a hard spheroidal mass, which is maintained above the vestibule of the larynx by the infiltrated and inextensible aryteno-epiglottidean folds, and the functions of the larynx are gravely compromised (Jeanselme). The epiglottis may be markedly involved and the rest of the larynx escape. Similar changes may occur in the arytenoid cartilages. A peculiarity of this locality is that but one side may be involved.

Next in frequency to the preceding, the glossoepiglottic and ary-epiglottic folds are involved and in a similar manner. The true cords frequently exhibit swelling and thickening which may in time lead to ulceration, and later may involve an entire cord. The tendency of the ulcers to cicatrize is very marked, and not only the true but the false cords may be destroyed. As a result of the ulcerative process the structures of the larynx are often changed into a shapeless mass at an advanced period of the disease. These changes induce hoarseness up to complete aphonia and at times dyspnœa.

Attacks of dyspnœa from laryngeal stenosis are not uncommon.

They may result suddenly from an acute œdema conjoined with an acute laryngitis from exposure to cold, attended with suffocative symptoms and cyanosis, or they may develop more gradually from the thickened, vegetating, and pachydermatous condition of the mucous covering of the larynx.

Alterations of the voice are quite common during all the stages of leprosy. The significance of this change was known at the time of Moses; the priest recognized the leprous by commanding them to speak before him. The voice may be harsh, raucous, nasal, or otherwise altered in its timbre. In other cases the voice becomes thin, feeble, or there may be aphonia more or less complete.

According to Jeanselme the functional disorders of the voice may be produced by two mechanisms. Sometimes they result from closure of the glottic opening by some material obstacle (deposit of tubercles on the laryngeal mucous membrane, destructive lesions of the vocal cords, interarytenoid pachydermia); at other times they are the consequence of an insufficiency of the glottis, the vocal cords leaving between them an aperture during the emission of sound. This paralysis of the vocal cords appears to be determined by a neuritis of the recurrent laryngeal nerve. Lesions of the cartilaginous portion of the larynx occur at a later period of the disease, resulting at times in necrosis of the cartilage. The laryngeal stenosis is often so pronounced that tracheotomy is necessary to prolong the life of the sufferer. All observers note the analogy between leprosy and tuberculosis of the larynx.

Leprous Affections of the Eye.—The frequency with which the eye is affected in tubercular leprosy is variously estimated at from sixty-six to seventy-five per cent. Even a larger proportion is given by some authorities. As the leprous process almost always begins in the oculopalpebral mucous membrane, these affections may properly be considered under this head. At an early stage of the disease, according to Daniellsen and Boeck, the white of the eye assumes a muddy appearance and the vessels of the cornea are seen to be periodically injected. This change of color gradually increases and usually produces upon the sclerotic towards the exterior border of the cornea a grayish-yellow thickening, which forms around the cornea a rampart of more or less elevation. The thickening progresses simultaneously with an increase of vascular congestion until the whole conjunctiva becomes the seat of the specific infiltration. There is an erythematous swelling of the eyelids, the eyelashes fall, and permanent induration may remain along the tarsal cartilages, or the eyelids may be completely invaded by leprous tubercles. The disease eventually extends from the sclerotic to the cornea. The original infiltration,

which may now be called a tubercle on account of its increased volume, acquires a brownish color, is firm to the touch, and extends through the thickness of the cornea. After having penetrated through the cornea the tubercle reaches the iris, which then assumes a dirty grayish color, the growth eventually passing into its substance. The pupil becomes irregular and the anterior chamber is gradually filled with tubercular matter. The patient feels lancinating pains in the eye and the sight is extinguished. The disease progresses up to the complete occupation of this chamber and the invasion of the entire cornea by the yellowish-white matter. The eye is then a shapeless mass. There is produced a sort of staphylomatous tumor which increases to such an extent that the eyelids no longer cover it. After a time the tubercular mass softens, the tumor contracts, and the eye can again be closed.

Instead of this mode of invasion the iris may be, according to Leloir, independently and primarily involved, constituting a leprous iritis and resembling certain forms of syphilitic gummous iritis. The tubercle penetrates into the posterior chamber, producing posterior synechiæ, and extends over the anterior surface of the crystalline lens. It sends prolongations into the anterior chamber, which may unite with prolongations of the tubercles which have invaded the cornea. The almost invariable termination of this leprous iritis is loss of sight. At other times there may be a diffuse lesion of the iris, iridocyclitis. According to Hansen, thirty per cent. of tubercular lepers have lesions of the iris.

These ophthalmic lesions may be acute or subacute in their evolution, but the almost invariable termination is partial or complete loss of vision. According to Hardy, the ulcerated surfaces of the eyelids may contract adhesions with those of the sclerotic, and the eye is then immobilized in its socket.

The *genital mucous membranes* may also be the seat of leprous lesions. The balanopreputial, or the vulvar, and the anal mucous membranes are sometimes involved and then become the seat of tubercles.

Period of Ulceration.

We have seen that, in their ordinary evolution, the leprous tubercles come out in successive crops, usually preceded by febrile attacks; that the earlier tubercles are usually resorbed or ulcerate and may entirely disappear; and that the disappearance of one group is succeeded by another in the same or new regions at variable intervals. After they have attained a certain degree of development the tubercles may remain for weeks, months, or years without retrogress-

ive changes, but, eventually, as in the case of other new formations of the granuloma type, the leprous tubercle shows a tendency to disappear by resorption or fibroid degeneration, or by softening, breaking down, and discharge of its contents. The one process is essentially curative and healing, the other destructive.

The stage of ulceration marks a period in the life term of the neoplasm. Undoubtedly many tubercles ulcerate as a result of external injury, but in most cases the ulcerative process occurs as a natural phase of the evolution of the disease. It is held by some that the non-viability or inaptitude for permanent organization of the tubercles is caused by the gradual accumulation of the bacilli in the perivascular spaces and the obliteration of the vessels, when the neoplasms, being deprived of their blood supply, undergo necrobiotic changes. Central mortification is first noted in the skin, which softens in the centre, breaks, and gives exit to the contents of the tubercles.

The capability of the lepra bacillus to induce suppuration by its presence is undetermined, and it is a question what is the rôle, if any, the pyogenic microbes play in the production of the suppurative process. Impey thinks that suppuration of the inguinal glands and other ganglia occurs through the action of pyogenic cocci and not through that of lepra bacilli. In one form of ulcerative lesion, *mal perforans*, the lepra bacilli are absent.

Fibroid Degeneration.—In many cases the neoplasms undergo a sort of fibroid degeneration. As a result of frequently recurring congestive processes there is a formation of connective tissue, and a fibrous metamorphosis is effected in much the same manner as in certain tuberculides (*lupus sclèreux*). The repeated congestive attacks result in the formation of cicatricial tissue, which limits the multiplication of the bacilli and is essentially a conservative element in the disease. This fibroid degeneration is marked by a diminution in the volume of the tubercle; it becomes smaller, firmer, and more indurated. On section of the tubercle it is seen to be composed almost entirely of fibrous tissue, which renders it inapt for the germination of the bacilli. These sclerosed tubercles are frequently permanent and may become keloidal. When this fibrous transformation occurs in all the tubercles, the disease is said to be arrested.

The same fibrous transformation may occur in the diffuse infiltrations (*lepromes en nappe*). The surface becomes browner, with increased desquamation. Gradually the infiltration in its entire extent becomes resorbed, leaving a superficial pigmented cicatrix. It has been observed that this change may take place coincidently with, or as a result of, an attack of erysipelas.

Interstitial Resorption.—In some cases the tubercles having attained a certain degree of development, a retrogressive process takes place without open ulceration; the tumors disappear by a process of interstitial resorption. The upper portion of the nodule becomes less prominent, often sinking in the centre, giving it an umbilicated appearance; and there is a progressive diminution of this central portion of the nodule until only a narrow circular wall of infiltration is left, which finally disappears, leaving a grayish or brownish pigmented cicatrix.

Ulceration.—The ulcerative process varies accordingly as the necrobiosis involves the centre or the totality of the tubercle. In the former case the skin over the centre of the tubercle becomes softened, and one or more yellowish points are seen which soon open and discharge a thick viscid or purulent yellow matter, which concretes in greenish, brownish, or blackish crusts, resembling the crusts of syphilitic ulcers. The ulcer is round, irregular, the edges are often perpendicular or undermined, the base is reddish-brown, grayish, or pseudomembranous, sometimes fungous, secreting a sanious pus. These ulcers are indolent and may persist for months or years practically unchanged.

In other cases in which the totality of the tubercle is involved in the suppurative process the entire neoplasm disappears by purulent dissolution, and the contents are discharged en masse, as in an abscess. The cavity may remain open for a long time, with a resistant infiltrated wall, and the crateriform ulcer thus left as a rule cicatrizes, leaving a slightly depressed, wrinkled cicatrix. Not infrequently two or more ulcers may unite to form a large irregular ulcer; or the whole body may be the seat of these disfiguring ulcers and crusts. Leprous ulcers seem to heal with remarkable facility under the influence of rest and aseptic dressings, and the extensive cavities are filled with cicatricial tissue. The resulting cicatrices are hard, irregular, often white in the centre, and surrounded by a brownish ring of pigmentation.

This cicatricial tissue may afterwards become the seat of tubercles. It is to be noted that the development of new tubercles is often synchronous with the ulceration and disappearance of old ones. While certain tubercles are being eliminated by ulceration and subsequent cicatrization, new tubercles appear which soften and ulcerate in their turn.

The course and character of the leprous ulceration are modified according to its situation and also by the intercurrent processes of erysipelas-like inflammations and gangrene. Tubercles on the extremities are more apt to break down into ulcerative lesions, as, for example, upon the dorsal surfaces of the feet and ankles, the legs, backs of the hands and forearms, and the face. When an ulceration is about to

occur in these localities, the skin becomes swollen, and in this infiltrated skin violaceous, livid spots form, which open in a few days and discharge an acrid, viscid material.

The occurrence of ulceration on the lower extremities is determined partly by dystrophic conditions here present in the shape of marked œdematous infiltration—a hard, brawny, pachydermatous condition of the integument which is sometimes so pronounced as to suggest elephantiasis arabum. The contusions, injuries, and various traumatisms to which lesions in these localities are subjected, as well as lack of cleanliness, doubtless act as exciting causes. The ulceration rapidly extends and may involve the intervening tissues and surrounding surfaces over a considerable area. It may advance around the limb, like varicose or syphilitic ulcers of the lower extremities, or cover the entire dorsal surface of the feet and ankles. The ulcerations are sometimes quite extensive both in area and depth. They may take on a gangrenous action and cause profound loss of tissue, sometimes ploughing up the soft tissues and laying bare the ligaments and bones, with necrosis consecutive to the osseous denudations.

The destructive changes which occur at this stage of the disease in the nasal fossæ, palate, larynx, and trachea have been considered in connection with leprosy of the mucous membranes.

It has been observed that intercurrent acute diseases may produce a temporary subsidence of the tubercles. After an attack of erysipelas, smallpox, or other acute infectious disease many tubercles often disappear. The beneficial effect of these intercurrent inflammations has been explained on the ground that they alter the blood supply to the part, while at the same time they favor absorption. Reference will be again made to these points in connection with the complications of leprosy.

Termination.

As leprosy advances in its evolution, all the symptoms increase in intensity and severity. In connection with the ulcerative processes, evidences of profound cachexia are usually manifest, due to leprous deposits in the viscera or amyloid degeneration of internal organs. Unless the unfortunate patient is carried off by some intercurrent disease, he may live for years suffering a slow and progressive decomposition of the body through the breaking down and ulceration of the organs invaded by the leprous deposits.

The chief causes of death are usually tuberculosis, enteric complications with colliquative diarrhœa, exhaustion from ulceration and gangrene, renal disorders resulting in dropsy, pulmonary lesions, suffocation from œdema of the glottis, or stenosis of the larynx or tra-

chea. The visceral complications have been generally regarded as tuberculous in character, but it has been suggested by Arning that we have been mistaken in attributing deaths of lepers to intercurrent pneumonias, phthisis, and dysentery, which were simulated by the clinical symptoms.

Although leprosy is regarded as among the most fatal of all diseases, however paradoxical the statement may seem, the leper seldom dies of leprosy.

According to the tables of Hillis, thirty-eight per cent. of lepers die of internal leprous deposits, marasmus, atrophy, suffocation from œdema of the glottis or laryngeal stenosis, or exhaustion from leprous ulceration, which may be the immediate consequences of the disease itself. This proportion of deaths due directly to leprosy is probably too high. Lepers commonly die of terminal infections which have no necessary connection with the disease, as albuminous nephritis, phthisis, bronchitis, pneumonia, diarrhœa, etc.

That tubercular leprosy progresses to a fatal termination is a rule to which there are few exceptions. There have been cases, exceedingly rare, in which the tubercles have entirely disappeared, the ulcerations have healed, and there has been a definite cessation of all further manifestations. The fires of the disease have apparently burned out, and the patient lives for years, showing in his scarred and disfigured features the traces of the destructive process which has swept over them, and finally dies of some independent disease.

Daniellsen reports three cases of permanent arrest of the disease, in one of which there had been complete exemption from all leprous manifestations for thirty years. In another case, that of a woman, the cure had been complete for twenty years. Kaurin reports a case in which there was a complete disappearance of the tubercles with apparent cure which persisted for many years, the patient finally dying of cerebral hemorrhage at the age of ninety-five. The autopsy showed no evidence of the bacilli in the integument or internal organs. In another case there was a complete disappearance of all accidents for twelve years or more, the patient remaining in good health. Cases of real and apparent cure have been reported by others.

It is well, however, to distrust the authenticity of many cases of reported cures, unless a considerable lapse of time has ensued after the disappearance of all accidents. The disease may reawaken into activity after a long period of exemption from all manifestations and new tubercles form, or, as it sometimes happens, after the ulcers have entirely healed there may be what is termed a visceral metastasis, a determination of the morbid process to the lungs, liver, kidneys, or some other important organ, which soon leads to a fatal ter-

mination. The most hopeful prognosis justified by observation of the usual course of the disease is that the tubercular leper may become an anæsthetic leper.

Cases of metamorphosis of the tubercular into the anæsthetic form are by no means rare. The pathological explanation of this transformation would seem to be simply a migration of the bacilli from the integument into the previously immune nerve tissues. In many cases of advanced tubercular leprosy, this transition is shown by the supervention of anæsthesia, atrophy, and other symptoms peculiar to anæsthetic leprosy.

In one class of cases there seems to be a merging or rather a passage of the one form into the other by almost insensible gradations. Coincidently with the disappearance of the tubercles and the healing of the ulcers there is the appearance of the characteristic symptoms of the anæsthetic form: atrophies, paralyses, enlargements of the nerves and consecutive trophic troubles in the shape of deformities and mutilations. Leloir has sometimes observed that in old tubercular leprosy which had become associated with nerve leprosy, the skin, subcutaneous tissue, and muscles of the face acquire a gelatinous appearance and trembling due to a kind of colloid degeneration.

In other cases, instead of this gradual transition of one form into another, the tubercles disappear completely and the patient seems cured of his leprosy. After a period of exemption from all accidents there may be a macular eruption, followed by the regular evolution of symptoms of anæsthetic leprosy, precisely as if there had been a fresh infection. Daniellsen has observed a case of this kind in which, six years later, the anæsthetic form was still maintained with all its characteristic features.

Complications and Conditions Influencing the Course of Leprosy.

Leprosy may be complicated with various parasitic and other affections of the skin, as scabies, favus, ringworm, eczema, psoriasis, etc. The incidence of these affections is much larger in tropical countries, where a greater surface of the body is habitually exposed and where parasitic affections of the skin are more common and of more luxuriant development. It is sometimes difficult to discriminate between the incipient manifestations of leprosy and chromophytosis and other parasitic affections.

Daniellsen and Boeck say that in Norway leprosy is almost constantly complicated with some *chronic cutaneous malady*, the most common being Norwegian scabies. Besides introducing an element

of confusion in diagnosis, the breaks and excoriations of the skin which commonly attend these parasitic dermatoses are considered to afford favorable spots for the entrance of the leprous virus and thus constitute an important agency in the propagation of the disease. Under the improved hygiene which has taken place in recent years this complication is not at the present time nearly so frequent as formerly.

The foramina contagiosa effected in prurigo, eczema, and other parasitic dermatoses, by scratching or wounding the integument, are regarded by Hebra and others as channels of entrance of the bacilli into the system.

The complication with *yaws* or frambœsia and also with *elephantiasis arabum* has been noted in countries where these diseases exist. It is a matter of some scientific interest perhaps that elephantiasis arabum is very common in the Samoan Islands, where leprosy is, or was a few years ago, unknown, while the former disease is not met with in the Sandwich Islands, where leprosy is so prevalent.

Leloir was impressed with the remarkable coincidence of *goitre* and leprosy in Italy. Among twelve Italian whom he observed in the north of the peninsula, six were affected with goitre.

Syphilis often complicates leprosy. In a number of cases which have come under my observation in the Charity Hospital of New York syphilis was also present. Each disease, however, seems to run an independent course, although it has been said that the tertiary accidents of syphilis are rarely seen in syphilitic lepers. The antecedents of lepers are often syphilitic, and this is regarded by many as constituting one of the most important predisposing causes of leprosy. The native population of the Sandwich Islands was at one time almost decimated by syphilis, and the impaired constitutions resulting from these syphilitic progenitors, coupled with the feeble capacity of resistance of the native Hawaiians, has always been regarded as among the chief causes of their remarkable susceptibility to leprosy and its rapid spread among them.

The similarity of the two diseases in certain objective characters and their frequent coincidence led to the erroneous opinion that leprosy was a modified syphilis or, as it has been termed, "a fourth stage of syphilis." The broad lines of distinction between these two diseases are, however, too obvious to merit special mention.

Impey describes under the title of "Syphilitic Leprosy" a form of the disease which he regards as worthy of separate designation. "Though produced by the combination of two distinct diseases, yet each malady modifies the other in such a marked manner that the distinctive characters of the primary disease are lost in the combined diseases." He says that in these cases of syphilitic leprosy "the

mouth and throat become much affected, the hair is removed from the scalp in large patches, bones in various parts of the body become necrosed, lymphatic glands are enlarged and often suppurate. Indolent abscesses are formed in various regions, the bones of the nose are soon lost, and the nose itself is soon removed by ulceration; these symptoms being almost entirely due to the syphilitic poison. When to these disfigurements the deformities of leprosy are superadded, the symptoms produced are almost too terrible to behold," etc.

Tuberculosis may also complicate leprosy, in some cases constituting the primary affection upon which leprosy has been engrafted. More commonly, however, tuberculosis represents a terminal infection and is the chief cause of death from its visceral complications. In his investigations of leprosy in Norway, Leloir was struck by the enormous number of persons affected by scrofula, tuberculosis, anæmia, and chlorosis in the leprous regions he visited. The coincidence of the scrofulous diathesis with leprosy determines a marked modification in the character and course of the leprous manifestations. Many observers agree that scrofula exercises a certain influence on the leprous tubercles which take on a "scorbutic appearance." Leprosy occurs very often in persons of scrofulous and tuberculous antecedents. Verteuil, quoted by Leloir, has often noted the coincident occurrence of pulmonary phthisis and leprosy in families. In a European family of eight children, two of the boys died of leprosy, and the third boy and two sisters succumbed to pulmonary phthisis.

The eruptive fevers exert a marked influence upon the course of the leprous process. An attack of typhoid fever, pneumonia, etc., may cause the rapid involution of the leprous lesions, which may not reappear for a long time. Hardy speaks of the good effects of an intercurrent attack of smallpox. *Vaccination* is sometimes said to exert an equally favorable influence. Beavan Rake particularly noted first swelling and then disappearance of the tubercles in patients whom he had vaccinated.

In the case of the acute infectious diseases, there seems to be a sort of antagonism between the newly introduced parasites and those of leprosy. The former, temporarily at least, dominate the pathological field and prevent the development and multiplication of the lepra bacilli.

The salutary influence of an attack of erysipelas in causing the disappearance of leprous manifestations has been attested by many observers. The curative action of erysipelas, as in other infectious diseases, is not as a rule durable, but causes only a temporary interruption to the course of leprosy.

An acute attack of pulmonary phthisis may also arrest and render

stationary the course of leprosy. Leloir found that it caused the disappearance of the cutaneous tubercles. In this class of cases there is simply the introduction of a new pathogenic factor which, as it is more acute in its development, takes precedence for the time being.

Malaria would seem to exercise a most unfavorable influence upon leprosy. It has been noted that the course of the disease is more rapid and severe in persons who live in low, damp dwellings exposed to marshy and malarial emanations. It has also been observed that the removal of a leper to a non-malarial region is almost invariably followed by an improvement of at least temporary duration.

Cold and Change of Season.—Undoubtedly the course of leprosy is influenced by the change of seasons, especially in latitudes where temperature changes are sudden and severe.

Cold seems to exercise a special excitatory influence upon the leprous process. The relation between the so-called "congestive attacks" or exacerbations and cold has been remarked by numerous observers. There can be no doubt that cold in some way or another exacerbates the disease. My observation of a number of leprous patients goes to show that in this climate they are better in summer than in winter. With the approach of colder weather in September and October, many of the symptoms which had entirely disappeared or were in abeyance during the summer begin to revive and become aggravated, and this irrespective of the type of the disease.

This seasonal exacerbation of leprous symptoms represents another of the numerous analogies of the disease with tuberculosis. The reason why patients suffering from pulmonary tuberculosis are better in warm than in cold weather is not far to seek, but why aggravation of the tuberculous process, irrespective of the localization of the tubercles, should take place in cold weather is not so evident. Hutchinson's testimony is that lupous patients get better in summer and grow worse in winter.

One reason why the more virulent tubercular form of leprosy predominates in cold climates may be due to the fact that cold more than any other external factor favors the growth and multiplication of the bacilli.

Anæsthetic Leprosy.

The anæsthetic form presents a characteristic variety and complexity of symptoms. It possesses a physiognomy peculiarly its own, and its clinical aspect is so entirely different from that of tubercular leprosy that it is difficult to recognize it as a form of the same disease due to the action of an identical pathogenic factor. The phenomena are essentially those of multiple neuritis, consisting princi-

pally of disorders of sensation and nutrition. The trophic troubles which are consecutive to the lesions of the peripheral nerves are distinctive of this form of leprosy.

The *period of incubation* is usually more prolonged, which may be due to the small number of bacilli or the greater resisting-power of the organism to their inroads. Its onset is gradual and insidious, and the prodromes are distinguished by the absence of febrile symptoms, as a rule, and the more pronounced character of the subjective symptoms of hyperæsthesia, pruritus, and pain.

Cutaneous Manifestations.

The Erythematous Eruption.—The first cutaneous manifestation of nerve leprosy is usually in the form of a localized erythema. Exceptionally the initial lesion may be in the form of bullæ. In two of my cases the formation of bullæ preceded by several months the appearance of any macular lesion. The appearance of the macular exanthem is so constant a phenomenon that Hansen proposed substituting the title "macular" for anæsthetic leprosy; yet it is to be observed that in certain cases the macules may be entirely absent and the inital symptoms consist of motor and sensory paralyses.

While the cutaneous eruption in nerve leprosy is perhaps not so essentially a part of the morbid process as in tubercular leprosy, which is localized in the skin, the macules exhibit a greater variety of aspect, especially in their configuration and coloring. This is due largely to the fact that instead of being transitory and evanescent, they usually remain permanently and show a tendency to increase by peripheral extension while clearing in the centre, and also to the fact that more pronounced pigment changes occur during their evolution. The macules may be simply erythematous, afterwards becoming pigmented or achromatic, or they may be pigmented or achromatic from the first, without preceding hyperæmia or congestion.

The first appearance of the eruption often follows exposure to cold or damp. Many persons date its origin to a cold, and it is usually preceded by a sense of formication, tingling, burning, or stinging. The spots may develop without any subjective sensations, the patient discovering them by accident. In persons who are not observant or when the spots appear upon the covered portions of the body, they may exist for a long time without the knowledge of the patient. In the patient, whose face is portrayed in Fig. 7, there was upon the dorsal surface of the foot a large discrete red patch, which from its size and other objective characteristics must have existed for a long time and which the patient discovered by accident. In another

case I found large patches upon the buttocks, of the existence of which the patient was ignorant.

The efflorescence may resemble polymorphous erythema upon its first appearance. The macules are usually circular or oval in outline, or they may be irregular in shape (Fig. 6). They vary in size from that of a finger-nail to that of a silver dollar or larger. They are usually small on their first appearance, but slowly increase in size. Their contour is gradually lost in the coloring of the surrounding skin, so it is impossible definitely to define their limits. In some cases they exhibit sharply defined dentate margins, as seen in Figs. 6 and 7.

Fig. 6.—Macular Lesions of Anæsthetic Leprosy.

The color of the erythematous spots varies from a delicate pink or red to a yellowish or bluish-red color, which later may deepen into a brownish-yellow, slaty, or black shade. The gradations depend largely upon the race and complexion of the individual and the chronicity of the patch. As they grow older they exhibit a greater variety of tints.

In many cases the redness may be so little pronounced that the patient does not perceive it; it disappears on pressure, to reappear immediately. It may fade out temporarily, leaving a grayish or yellowish tint. Friction, heat, and cold, especially cold, accentuate it. I have found that patches may be well defined by the application of

cold water to the surface. In the earlier stage one may observe the dilatation of the cutaneous capillaries; later these spots may become brown or black, constituting one of the forms described by early writers as *morphœa nigra*.

The achromatic patches may result from the involution of the pigmented macules, or they appear at first as perfectly white patches upon the healthy skin (*morphœa alba*). This latter form is rarely seen in the white race; it is more common in dark races and in tropical countries. I have seen many examples in the Hawaiian lepers. Sometimes these decolorized patches are surrounded by a hyperchromatic margin.

The surface of the patches in the earlier stage is perfectly smooth. After their complete development there is more or less continuous desquamation from the surface of the patches, which is usually of a bran-like, furfuraceous character. In rare cases, when there is great disturbance of the circulatory equilibrium, the epidermis may peel off in large lamelliform flakes.

The hair of the affected surfaces often becomes white or falls out, although the bleaching of the hair is not nearly so common or constant a phenomenon as has been described by many writers. There is a more or less complete suppression of the sweat secretion, not only of the anæsthetic patches, but sometimes of the skin immediately surrounding them, so that the injection of pilocarpine does not excite the glands into activity.

The patches may be the seat of a violent pruritus, which is accentuated by elevation of temperature and exercise, or they may become so hyperæsthetic as to give the sensation of a superficial burn. They may persist for years, constituting the only sign of the disease until the appearance of certain nervous symptoms indicates irritative or degenerative changes in the nerves.

Like the exanthem of the tubercular form, the macules have a predilection for certain regions of the body. Although the most frequent sites are upon the face, hands, and feet, especially about the ankles, they may appear upon the back, shoulders, chest, arms, nates, thighs, and abdomen. They are rarely seen upon the palms and soles, and most authorities concur in the statement that they are never seen on the scalp. This statement is subject to modification. In the case of the patient shown in Fig. 7, the eruption extends up over the frontal portion of the hairy scalp to the vertex, as is well shown in the illustration.

C. W. S——, aged 47 years, born in Bermuda. Mother living, in good health. Father died at sixty-five (twenty-two years ago), the patient states, of some kind of "skin disease" of many years' dura-

tion. His face was blotched, his lips were swollen, the lobes of the ears hung down, and he is reputed to have had syphilis. The mother and father had lived together forty years. The mother is now living, in good health, eighty-three years of age. Of the seven children, two brothers and two sisters died of lung trouble. The youngest child died thirteen or fourteen years ago, at the age of sixteen, from some form of skin disease. He had an eruption of the skin and swelling of the face for five years previous to his death.

The patient left Bermuda, at the age of seventeen years, to become a sailor. He visited the West Indies, the Mediterranean, was in hospital at Constantinople for a long while, and made several voyages

FIG. 7.—Leprosy Affecting the Hairy Scalp.

to Bombay and other parts of the East Indies. He also made voyages to various West Indian and South American ports. He came to New York in 1883, and has lived here since continuously with the exception of a few trips in a sailing-vessel down East.

The patient first noticed a spot in the middle of the forehead just above the root of the nose, sixteen years ago. It remained apparently stationary for a long time, and then began to spread gradually downwards over the nose, cheek, and upper lip, and upwards, involving the entire surface of the forehead and creeping up into the hairy scalp and downwards again to the junction of the chin with the neck. Three or four years ago it extended behind the ear and upon the left side. For years he had experienced stinging sensations in the face, and about six months ago he noticed a numb or "dead sensation," as he termed

it, over the entire region of the face. The eyelashes have entirely disappeared, but the eyebrows are intact. The distribution of the eruption over the right side of the cheek and forehead and extending up into the hairy scalp is seen in the accompanying illustration (Fig. 7). On the left side the patch has extended backwards behind the ear to a point half-way between the ear and the occiput, and the plainly defined hyperchromatic margin sweeps upwards in the hairy scalp, to join the patch on the right side shown in the picture; it extends downwards to the middle of the neck. There are two circular, palm-sized patches, one over the left deltoid region and one on the antero-lateral surface of the left leg, which were first observed eighteen months ago; the patient thinks that they were then about the same size as now. There is also a large circular patch beginning at the root of the toes and embracing within its area almost the entire instep of the right foot. The patient does not know when this patch first appeared. He noticed twitching of the muscles of the toes and the loss of feeling over the instep of the right foot twelve or eighteen months ago. At the present time this patch is almost completely anæsthetic. There is some enlargement of the peroneal and ulnar nerves. He has noticed for a year or more that upon awakening he finds the left arm asleep. This phenomenon occurred only occasionally at first, but now it is frequently observed in both arms. He frequently upon awakening notices the fingers of both hands asleep, the sensation being most pronounced in the little and ring fingers.

The patient had syphilis fifteen years ago, and an attack of gonorrhœa which infected his left eye and impaired the eyesight. He had epilepsy until twenty-five years ago. After an attack of yellow fever in 1863 or 1864 from infected clothing his epileptic seizures disappeared, and his general health has since been much improved.

The changes which occur in the evolution of the lesions give them a distinctive character. The macules may remain discrete or, spreading peripherally, form by their confluence irregular patches with polycyclic outlines, parts of circles (Fig. 8), or large gyrate patches with slightly elevated and distinctly defined margins and pale, pigmentless centres. The decolorization of the centres of the patches with the slightly raised hyperchromatic margin give sthem oftentimes a distinctly annular appearance. This process of blanching may extend over large surfaces of the body. Upon the limbs the patches often exhibit a serpiginous tendency, gradually extending up the limbs or spreading over the joints.

It will be observed that the centrifugal tendency which characterizes the extension of the lesions is also marked in the retrogressive process, which invariably begins in the centre. All the manifold changes of form which are observed in the macules of anæsthetic leprosy are effected by the gradual implication of the surrounding healthy skin by the advancing hyperchromia with the constant blending of their contours and their subsequent partial effacement.

The eruption is often symmetrical, but would seem to be independent of the distribution of particular nerves. In certain cases the maculæ are dispersed along the intercostal nerves, forming a double zona which is absolutely painless.

Eruption of Bullæ.—Allusion has already been made to the fact that a bullous eruption may be among the earliest cutaneous manifestations of leprosy; at a later stage of the disease it constitutes a characteristic and by no means uncommon symptom. The appearance of bullæ may be preceded by symptoms of general disorder, fever, and neuralgic pains, or they may develop without any premonitory symptoms. In one patient of mine bullæ appeared along the anterior lateral aspect of the right leg, one-half dozen or more in number, as the first cutaneous expression of the disease.

FIG. 5.—Macular Lesions of Anæsthetic Leprosy.

The bullæ vary in size from that of a small pea to that of a cherry or larger, and the individual lesions resemble somewhat in appearance those of pemphigus vulgaris. The epidermal walls are first distended by the effusion of a pale yellowish serum, and the bullæ may increase in size and their contents become purulent; they may undergo spontaneous rupture after a few days, and their flaccid walls may be wiped or brushed away, leaving slight reddish spots or slight pigmented stains which soon clear up.

Instead of this rapid involution the bullæ may increase in size, the

contents become purulent and concrete in the form of yellowish-green or brownish crusts, which when removed reveal excoriations more or less profound, and superficial ulcers; the latter, on cicatrizing, leave prominent scars which are at first pigmented and later become white, smooth, and shining and frequently bordered by a darkly pigmented ring. The blebs may succeed one another for several years or during the whole course of the disease without being accompanied by any notable disorder other than the neuralgic or rheumatoid pains. At a later stage the ulcers not infrequently persist, increase in area and depth, and constitute the starting-point of deep-seated ulcers and mutilations.

The so-called *lepra lazarine*, which is common in certain countries, as in Mexico, and which has been described by certain observers as a distinct form of leprosy, represents only a variety of this bullous eruption. There is in this phlyctenular eruption a slow formation of blebs which present the appearance of a slightly raised, parchment-like covering, involving the epidermis and superficial layers of the derma, which are distended by a serous accumulation (pemphigus escharotica). When this eschar is detached it leaves an ulcerated surface, with grayish fungoid base and perpendicular sides, which may either be persistent and extend in depth or be complicated with gangrene and lead to mutilation (Leloir).

The points of predilection for the bullæ are the backs of the hands and feet, heels, back of the elbow, and the anterior surface of the knees, although they may be found on any portion of the external integument. It is evident that these parts are more particularly exposed to rubbing and irritation from contact of all kinds. Impey believes that the bullæ are merely accidental phenomena caused by external injury and not essentially an expression of the leprous process. He asserts that they do not contain bacilli.

The results of the bacteriological examinations which have been made to determine the presence or absence of bacilli in the pemphigoid lesions of leprosy are contradictory. Kalindero, Petrini, Aristid Bey, and others assert that they have found bacilli, though in small numbers and not constantly, both in the crops of bullæ which come out spontaneously, and in the liquid secretions of the blebs which were produced artificially in lepers by the application of vesicatories. These results have been contested by other observers who failed to find bacilli in the bullæ. The general impression has always been that the bullæ of leprosy were caused by the action of the toxins rather than directly by the bacilli. Leloir has seen bullæ form in the mucous membranes.

Trophic Changes of the Glands.—Coincident with the development

of the patches certain changes take place in the glandular apparatus of the skin. These changes are first noticed in the surfaces occupied by the eruption, but later may affect the entire skin. The hairs of the affected surface suffer in their nutrition. The dystrophic change may be manifest in the bleaching or whitening of the hairs, which become thin, wasted, and lanugo-like, but may or may not fall out. A similar process of bleaching of the hairs has been observed by Weir Mitchell upon the hands and fingers in cases of "glossy skin." It has been noted that the hairs may reappear upon the patches from which they have disappeared. This regeneration is always coincident with other evidences of improvement in local nutrition.

The Sudoriparous Glands.—Reference has already been made to the abnormal activity of the sweat glands during the invasion period. This hyperidrosis is invariably succeeded by a diminution and finally a complete suppression of the sweat function. These anomalies are due to trophic changes in the glands, caused by the action of the bacilli or their toxins upon the peripheral nerves. Weir Mitchell has described a precisely similar condition in the "glossy skin" resulting from severe nerve injury, in which there was a marked hyperidrosis affecting the parts supplied by the nerve, followed by a complete anidrosis. The anidrosis is at first confined to the macular lesions and may be so complete that the injection of pilocarpine fails to stimulate their functional activity. The secretion is sometimes completely suppressed over the surface of the patches, while the surrounding skin sweats freely. I have observed, in a patch situated upon the heel and side of the foot, that while the central portion was absolutely dry, there was a hypersecretion around the peripheral border which appeared in the shape of small beads of moisture, while there was no sensible perspiration in the healthy surrounding skin. It would seem that in the evolution of some of these patches, the trophic changes are manifested in the central portion by achromia, anæsthesia, and anidrosis, while hyperchromia, hyperæsthesia, and hyperidrosis are marked at the periphery. After a certain period the sweat secretion becomes more or less diminished or completely suspended over the general surface of the body. In one of my cases there was observed, during the summer, marked hyperidrosis of the scalp, which was probably compensatory to a certain degree for the diminished secretion of the general surface.*

* On a visit to Molokai, several years ago, I observed this phenomenon in a very marked degree in two anæsthetic but not disabled lepers who carried my baggage to the top of the pali which shut in the leper settlement. After a fatiguing climb the sweat poured from the scalp and ran down their faces in little rivulets, while the perspiration from the hands, arms, and other exposed surfaces was hardly noticeable.

The sebaceous glands also become atrophied and altered in their function. The secretion, which was at first exaggerated, becomes entirely suppressed. At a more advanced stage, when the sweat and sebaceous glands are destroyed and there is a complete arrest of their functions, the skin of the general surface of the body becomes dry, parchment-like, and harsh to the feel. The epidermis readily cracks and fissures, and the breaks in its continuity not infrequently become the starting-points of superficial or deep ulcerations. It may be remarked that very often the skin of lepers, especially that of the hands, becomes dry, shiny, or glossy from atrophic changes, simulating the "glossy skin" of Paget.

Sensory Disorders.

For many years the cutaneous eruptions may constitute the only exterior manifestations of anæsthetic leprosy. But during this period and throughout the entire course of the disease there are certain modifications of sensibility which, in order to prevent repetition in their description, may be conveniently considered together under this heading.

In the ordinary conception of anæsthetic leprosy the most important clinical feature is expressed in the name by which this form of the disease is designated. While anæsthesia is an essential and fundamental feature of nerve leprosy, and indeed constitutes the most pathognomonic sign from a diagnostic point of view, there are numerous modifications of sensibility which are scarcely less interesting and important. In many cases the nature of the skin lesions is absolutely indeterminable without the indications furnished by the sensory disorders.

In many cases the sensory disorders constitute the only certain element of diagnosis, as is well illustrated in a case which came under my observation about ten years ago. The following notes were taken at that time:

In this patient the eruption began nearly five years ago as a small red, somewhat itchy spot on the anterior surface of the left foot at the base of the great toe. It enlarged slowly and almost imperceptibly. After a time it cleared in the centre while extending peripherally. At the present time it involves almost the entire upper part of the under surface of the foot. The hyperchromatic margin may be seen extending along the root of the toes and advancing with a circinate sweep along the outer aspect of the foot upwards to the ankle-joint, crossing the instep and continuing down under the instep and the inner half of the sole, and emerging upon the integument of the first phalanx of the great toe. The margin is irregularly scalloped, slightly elevated, one-quarter to one-half an inch in width, and of a

brownish or lilac tint. The central portion presents a bluish-gray tint, the coloration depending upon the atrophy of the skin, through which the superficial vessels are more apparent.

Upon the anterior inner aspect of the leg, at the junction of the middle and upper thirds, there is a patch two inches in diameter which began three years ago. The centre is faintly pigmented, the margin made up of brownish-red puncta, and partly of diffused redness. These minute points seem to represent infiltration of the follicles. This patch is anæsthetic in the centre. Above the external malleolus there are two irregularly circular macules, each about the size of a silver quarter, which made their appearance about two years ago. The centre is beginning to clear, though still pigmented, the margin is of a deeper, more brownish-red. But slight impairment of sensation can be detected in these more recent patches.

In the central portion of the older patch there is complete loss of the pain and temperature sense. The tactile sense is but slightly impaired, and the muscular sense is apparently unchanged, while just beyond the hyperæsthetic, hyperchromatic margin normal sensibility is preserved in absolute integrity. Were it not for the element of anæsthesia, I believe it would be impossible to diagnosticate the nature of this eruption. This patient has apparently entirely recovered.

We have seen that the invasion period is characterized by hyperæsthesia, pruritus, neuralgic pains, and other symptoms which indicate that the nervous system is the primary seat of the disease. The pathological basis of these phenomena is now recognized to be a specific neuritis, parenchymatous and interstitial, which attacks the peripheral nerves and leads to their more or less complete degeneration. The sensory disorders of nerve leprosy are not, therefore, pure neuroses, but rather trophoneuroses, since they are always consecutive to irritation and degeneration of the terminal filaments of the cutaneous nerves or some portion of the sensory conducting apparatus. Recent investigations would seem to show that the primary action of the bacilli is exerted upon the nerve terminals, and as these constitute an integral part of the skin, the sensory disturbances may be regarded as due to trophic influences. The sensory disorders may be associated with trophic changes, or they may occur without obvious structural changes in the skin.

These modifications of sensibility may be divided, according to the usual order of their development, into (1) *exaltations of sensibility*, expressed in hyperæsthesia, pruritus, dermatalgia, and neuralgic pains; (2) *perversions of sensation*, which consist of various dysæsthesias, sensations of needles and pins, numb and dead feelings of the limbs, delayed or retarded sensation, etc.; (3) *abolition of sensation, more or less complete*, expressed in anæsthesia or disassociation of the modes of sensation, etc.

The first group corresponds to the period of irritation of the nerves which may be exceedingly prolonged in duration.

The second group marks the period which intervenes between the cessation of the irritative neuritis and the complete disorganization of the nerve fibres. The nerves are in a state of stupor in which the sensation is delayed but not extinguished. Even at this period there may be some evidences of disassociation of connected sensations.

The third group corresponds to the complete disorganization of the nerves which serve as a medium of nutrition and sensation. It may be practically indefinite in duration.

The first effect of the neuritis is irritation of the part supplied by the affected nerve and may consist of tingling, of formication, of a sensation of heat or cold, or of stinging or burning at the surface of the skin or along the course of the nerve. The sensation is sometimes likened to that caused by an abraded surface which is exposed to contact with air or water. One of my patients would take off his shoe repeatedly, feeling sure that the smarting sensation felt along one side of the heel was due to the epidermis being rubbed off. One manifestation is in the form of localized itching, which frequently affects the palms of the hands or soles of the feet; it may occur in any portion of the limbs. It is apparently more deeply seated than in ordinary pruritus or in the pruritus of eczema. It is often persistent and tormenting and is relieved by grasping, compressing, or pinching the parts rather than by scratching.

The dermatalgia is sometimes described as a red-hot, burning pain. Any blow or pressure or even slight contact may cause a shock like that from an electric battery, which is felt to course along the affected limb. In one of my cases, upon merely rubbing the skin or slightly scratching over the anterior surface of the wrist, there was felt a tingling, radiating along the entire course of the forearm. This condition persisted for months.

In another case painful smarting sensations were felt over the anterior lateral aspect of the right leg in the immediate neighborhood of a pigmented patch. This continued three or four weeks and suddenly disappeared. All of these subjective symptoms may develop suddenly. They are exceedingly capricious, being manifest for a variable length of time and disappearing with the same facility with which they appeared. For weeks or months they may be entirely absent.

The hyperæsthesia is sometimes experienced in the greatest intensity in the face. Neuralgic pains may be felt along the course of the trifacial or along the ulnar, sciatic, and peroneal nerves, affecting the forearms, hands, the entire leg, feet, and toes. Locomotion is

often difficult and painful. The patient may feel as if he were walking on pebbles or broken glass. One patient describes the sensation "as if he were walking on stone bruises."

The pains instead of being superficial may be of a deep, boring, lancinating character, as if deep down in the tissues. They are paroxysmal in character and are particularly nocturnal. They may be so accentuated as to be atrocious, almost unendurable, depriving the patient of sleep, and the countenance often takes on an expression of habitual suffering.

As the irritative neuritis is succeeded by degenerative changes in the nerves, these exaltations of sensibility cede to a gradual dulling of sensation and more or less complete insensibility.

Many years may pass, and the patient, with the exception of outbreaks of new eruptions of macules or bullæ and occasional neuralgic pains, may have no disorders of sufficient importance to awaken his suspicions as to the exceeding gravity of the disease with which he is afflicted. During this period there are usually observed inflammation and enlargement of the peripheral nerves which become more pronounced as the disease progresses.

In the invasion of the nervous system the bacilli seem to manifest a predilection for the ulnar and peroneal nerves. The nerves which are most constantly and characteristically involved are the ulnar, peroneal, and median. Second in point of frequency are the facial branches of the seventh pair and the first division of the fifth. It is worthy of note that the nerves primarily involved are those which are most superficially situated and therefore most exposed from their situation and surroundings to external influence.

Why the bacilli show a predilection for certain nerves—the ulnar, for example, instead of the radial—has not been determined. The ulnar nerve is not invariably the first to be affected, and the bacilli may begin their depredations in any particular branch of the predilected nerve. The thickening of the ulnar nerve which may often be felt behind the olecranon, giving the sensation of a tense cord rolling beneath the fingers, is one of the earliest and most valuable signs of nerve leprosy. In doubtful cases, when other symptoms are equivocal, its presence furnishes the necessary confirmation of the diagnosis.

The interstitial neuritis may manifest itself in the form of a diffuse uniform enlargement, and the nerve may attain the size of the little finger. The thickening may be fusiform or more nodular or moniliform. This, according to Leloir, is characteristic of the ulnar modification. It is exceedingly sensitive to the touch, and pains may be felt radiating along its course to the fingers. At a later stage, when degeneration is complete, it does not permanently conserve its vol-

ume. There is a diminution, not only in size, but in sensitiveness. It may be forcibly compressed without provoking radiating pains in the region of its peripheral expansion.

For a long period there is noticeable a disposition of the hands to go to sleep, at first from pressure from lying upon them; later the numb sensation may occur without this pressure. This tendency of the limbs to go to sleep is especially marked at night, possibly from greater exposure to pressure of the arms from the posture assumed in lying. The patient wakes from a sound sleep finding, it may be, the little and ring fingers closed and asleep. At another time the fingers supplied by the median may be found closed and numb, and again the fingers of the entire hand. Similar sensations are often felt in the toes, more often in the great toe than in the small toes. It is noticeable that they return to the normal condition without the sensation of "pins and needles." In one of my patients the awakening was described as waves of sensation passing along the forearms into the fingers. Usually upon extending and flexing the fingers several times, sensation returned more or less promptly. At a later stage the patient, on awakening, found the fingers flexed and absolutely insensitive, and it was necessary to use the other hand to overcome the flexion. After working the fingers for a few minutes backward and forward sensation returned. It is evident that this sensation of numbness and deadness is to be differentiated from anæsthesia, as the patient is conscious of it from his own feelings. A patient does not know he is anæsthetic until it is revealed to him by some means outside of his own consciousness.

During this period the acuity of the tactile sense is dulled, and pins and small articles cannot be easily picked up. Articles are readily dropped, from tremor or weakness or inability to hold things firmly by the hand. The fingers lose their deftness for any form of mechanical technique. There is marked evidence of muscular atrophy and disturbance in the coordination of the muscles. The handwriting becomes changed, jerky, tremulous, and irregular. In performing any manual work which requires dexterity, the patient cannot do it from force of habit, and the guiding and directing influence of the eye must be applied for its proper accomplishment.

Hillis, whose careful personal study of leprosy in British Guiana gives his observations an especial value, says that many of the negro field laborers have their attention first directed to their condition owing to the difficulty they find in holding a cutlass. This, he thinks, is not so much from loss of sensation in the parts as from a want of coordinating power or muscular weakness, which amounts in some cases to a general tremor or shaking of the limbs. "Shooting

pains or an undue sensitiveness are nearly always felt in the fingers and toes before these parts are affected." In a case reported by Thin, a butcher suffering from nerve leprosy stated that the first symptom he observed in himself was a strange loss of power, as he expressed it, when cutting meat in the market. In another case, reported by Dejerine, a French soldier who had served for eighteen months in the Tonquin was discharged from the service for inability to handle his gun.

Another phenomenon which marks the transition into complete insensibility is retardation of sensation. It has been observed that in applying the electric current there may be quite an appreciable time before the sensation becomes distinct. The sensation does not at once attain its maximum, but gradually gains in intensity during twenty or thirty seconds.

With this slowness in the transmission of sensation certain perversions of sensation may be associated. Jeanselme found that if a hot body or a piece of ice is applied over a patch it causes at first the simple impression of contact. If the experiment is continued, a sensation of heat or cold is finally felt, feebly and only after a long time. If now, on the part where the ice has been, a moderately cold substance is applied, the patient is deceived and complains of a sensation of heat.

It is through this transition stage that the nerves pass into a stage of complete insensibility. Anæsthesia develops gradually. It is commonly noticeable at first in the patches, especially over the decolorized centres, and is often coincident with hyperæsthesia of the hyperchromatic borders. It may develop in regions not the seat of the patches and so insensibly that the patient is not aware of it. The patient does not feel the objects he grasps. He may not feel the heat of the pipe held in his hand or cuts made in shaving. One may stick a pin or needle into the patch without the patient's knowledge. In walking, the sensation has been compared to stepping on cotton, wool, or a thick carpet. The patient may walk barefoot on rock, gravel, or thorns without feeling the wounds they make. The insensibility is so complete that grave operations may be performed without any sensation of pain. Instances have been known in which the patient has chopped off the finger or toe which annoyed him without feeling pain.

Many of the cutaneous lesions encountered in nerve leprosy before the mutilating stage sets in are due to the suspended sensibility. The deadened nerves give no warning through the perception of pain to the inroads of heat, cold, or other injuries. The patient often receives a severe injury, or a knife may be thrust into the anæsthetic patch without any sensation being caused.

Sensibility to puncture is variable, not only in different parts, but in contiguous spots; the same is true of sensitiveness to temperature. Quinquaud found by means of a very delicate æsthesiometer combined with a dynamometer that, while 5 gm. in one point would elicit distinct sensation, it would require 100 gm. 2 mm. distant from the first point, to call forth the same degree of feeling. With regard to temperature, it was sometimes necessary to obtain 30° C. before obtaining a sensation; or 0° C. and 10° C. would be contiguous findings. There were frequent phenomena of disassociation. Some patients had no perception of cold, but felt heat, and vice versa. Analgesia and thermo-anæsthesia may be present with or without impairment of the tactile sense. While the loss of the pain sense is often so complete that the thrust of a pin into the affected part may occasion no pain, simple contact by gently rubbing the surface may be readily appreciated. This disassociation of the modes of sensibility is characteristic of leprosy.

The individual independence of the different modes of sensation which are normally connected is established by studying cases in which each of them appears isolated. In the anæsthetic patch of leprosy we find that a certain part of the skin cannot discriminate between heat and cold, another part is deprived of the sense of touch, and that though a third part may have the sense of feeling injury to it does not cause pain. It is worthy of note that hyperæsthesia may be manifest at an advanced stage of the disease, and it is frequently present in close proximity to the region that is absolutely anæsthetic. I have observed a number of times in applying electricity that a current representing the full strength of fifty elements and of sufficient intensity to char the tissues when passed through a wire brush, occasioned no sensation of pain in the central portion of the patch. In the zone just within the hyperæmic margin, one-half this strength would pass for a fraction of a minute without evoking any sensation, and then the nerve conductivity would be aroused, shown by a sharp sensation of pain, so that the strength of the current would have to be largely reduced to make it bearable. In the hyperæmic margin of the patch it required a smaller current to provoke sensation than upon the healthy sound skin.

It is worthy of note that while anæsthesia is the most durable symptom of nerve leprosy, sensation may return to surfaces formerly occupied by anæsthesia, or indeed it may very exceptionally be replaced by hyperæsthesia. The interpretation of the rationale of this retrogressive phase of the disease is not determined. It may be that not all of the fibres are destroyed and the power of conductivity which was held in abeyance is restored, or it may be that the nerve

fibres are regenerated and this restoration is followed by recovery of their physiological activity.

Jeanselme has made a special study of the mode of progression of anæsthesia, its topographical distribution, and its qualitative alterations, the results of which may be formulated as follows:

1. The distribution of anæsthesia in leprosy is manifestly symmetrical. When insensibility affects one member, it will soon attack the homologous member. In addition the anæsthesia is ordinarily distributed in an almost equal manner over the four extremities. Likewise the anæsthesia of the lower extremities is more extensive and more precocious than that of the upper extremities. In syringomyelia, on the other hand, the anæsthesia, often symmetrical, is generally predominant in the upper extremities; it may even be situated exclusively here.

2. Anæsthesia begins at the level of the free extremity of the members and mounts gradually upward to their root. Sensation, almost extinct in the hand or foot, is only dulled in the arm or thigh.

3. Anæsthesia of the deep parts of the derma is in general less marked and of later development than that of the superficial parts. As the anæsthesia progresses it descends lower and lower in the skin. At first the mantle of anæsthesia which covers the insensible region is quite thin; a needle pushed horizontally into the papillary body provokes no pain, but the patient protests as soon as the puncture involves the deeper part of the skin. Still later the skin becomes completely insensible and may be pierced entirely through without pain.

4. The anæsthesia, which is at first of ribbon form, tends to take on later the segmentary type. In the upper limb it occupies at first the little finger and the ulnar border of the hand, and forms along the postero-internal portion of the arm and forearm a long band; this ascends to a variable height, often to the elbow, sometimes to the axilla, the sensibility of which always remains intact.

In the lower limb the anæsthesia first affects the great toe and the internal border of the foot, sometimes the external border. At the same time a long band of anæsthesia commencing at the base of the leg ascends more or less high upon the external aspect of the leg, attaining the knee, the middle of the thigh, or even the region of the trochanter, upon which it widens *en raquette*. Sooner or later the primitive band of insensibility spreads out and forms a gutter, the two lips of which finally close together. The limb is then encased in a sheath of anæsthesia.

5. The segmentary anæsthesia of leprosy differs in its essential characters from the segmentary anæsthesia of syringomyelia. From an attentive observation of patients or from the indications furnished

by the first phases of the anæsthesia one arrives at the conviction that in its début the insensibility has been of the ribbon form.

6. The anæsthesia does not occupy the zone of peripheral distribution of a nerve trunk; the ribbon-like disposition seems to be determined by an alteration of the posterior roots or of the cord.

7. The anæsthesia of the face and of the trunk, without being rare in leprosy, is less frequent than that of the members. It does not form a mask or a vest neatly limited around the body.

8. In the beginning all the modes of sensibility are not simultaneously abolished; the thermo-analgesia far outstrips in its development the tactile anæsthesia. At an advanced period the imperfect disassociation of sensibility gives place to complete anæsthesia. Very often in the same subject the tactile anæsthesia is still frankly ribbon form while the thermo-analgesia has already reached the segmentary period.

9. If one applies or maintains during a certain time a hot or cold body upon a region partly deprived of sensibility, it is frequently the case that the patient complains of a double sensation; he immediately recognizes the contact, then after from five to eight seconds he perceives a feeble thermic sensation. This curious phenomenon is the consequence of a law that the more a sensibility is altered, the more slowly the sensation is produced. The number of seconds which elapse between the perception of contact and the perception of temperature expresses, so to speak, in figures, the degree of the alteration of the thermic sensibility.

10. In leprosy the sensitive perversions and the errors of localization are not rare.

11. The anæsthesia is not circumscribed within invariable limits. It embraces two zones: one fixed, which corresponds to the regions first and the most profoundly affected in their sensibility; the other mobile, at the level of which the sensibility is only in a state of stupor and not extinct.

Muscular Atrophy, Tendinous Retractions, and Deformities.

Atrophy of the muscular tissues and tendinous retractions give rise to various deformities, which are also pathognomonic features of nerve leprosy. Leloir says that muscular atrophy marches, in general, parallel with anæsthesia.

Among the induced changes is that of muscular atrophy accompanied by fibrillary contractions and marked diminution, ending in abolition, of the electric excitability.

The dynamometer shows marked diminution in the muscular con-

tractility. As the motor fibres are destroyed, proportionately to the muscular atrophy we have paresis and not paralysis as a resultant. Whether this is due to a lesion of the trophic fibres of the nerve or to loss of function by motor lesion is not known. In any case, pure motor paralysis is not met with in leprosy unaccompanied by lesions of the sensory and trophic systems. The muscular atrophy and tendinous retractions lead to conditions and deformations identical in appearance with those resulting from idiopathic nervous diseases.

The first sign of muscular atrophy is usually seen in the upper limbs. Commencing with the thenar eminence the atrophy involves the other muscles of the hands, particularly the interossei, and then extends to the flexors and extensors of the forearm and arm, affecting particularly the extensors. The hands become claw-shaped from the tendinous contractions; this deformation may correspond to the Duchenne type of paralysis. The hand becomes flattened, the muscular eminences disappear, the forced extension of the first phalanges giving a concave aspect to the metacarpal portion; the transverse diameter of the hand is narrowed. A man's hand may wither to the size of a child's.

The little finger is usually the first to become flexed, followed by the ring, middle, and index fingers, the thumb being usually the last. This order may be reversed; sometimes, but rarely, the thumb is the first flexed. In the production of the "leper claw" the proximal phalanges always bend backwards, while the middle and distal phalanges are curved inwards by the flexors. The first phalanges are thus in forced extension, the others in forced flexion. There may be, instead of the flexion of the thumb, a horizontal deviation by which it is curved inwards. The degree of contraction and the angle at which the fingers are flexed vary in different cases. In some cases only one or two of the fingers are flexed; in other cases the fingers become twisted on their axes and stand out at the most grotesque angles. In advanced cases the fingers cannot be straightened out by force. This tendency to flexion cannot be overcome by artificial means. Experiments have been made in straightening out the fingers and binding them on a flat board, nevertheless the process still continued.

The following case illustrates a characteristic deformation of the hand from tendinous contractions:

The patient, aged 20, is a native of the Sandwich Islands; father and mother both living in good health; when about eight years old he had a fall, sustaining a fracture of the right clavicle. For a long time afterwards he experienced a sense of soreness or lameness on the affected side. Within one to three years (the patient's testimony is not clear upon this point) he noticed a numbness of the hand, with

a tendency to contraction of the fingers. This gradually increased, becoming more pronounced. He was treated by the application of the actual cautery to the spine on the supposition that his trouble was of central origin. For the last several years the contraction of the fingers has remained unchanged, but the sensation of numbness has crept farther up the forearm.

Upon examination, he was found to be well nourished; there was some atrophy of the muscles of the right arm, more especially below the elbow; the deltoid was somewhat wasted; the circumference of

Fig. 9.—Characteristic "Leper Claw."

the right arm was one inch less than that of the left; there was also atrophy of the muscles of the right leg. The fingers were contracted, as shown in Fig. 9; over the knuckle of the index finger a superficial sore from slight traumatism had existed for several weeks without healing; the nails were thickened and deformed.

Over the lower half of the forearm and hand was entire absence of all sensation; from the middle of the forearm to the middle of the arm there was impaired sensation over regularly limited areas, extending higher on some aspects than on others; the temperature sense on the inner side of the arm was abnormal, hot water being mistaken for cold, etc. On the right lower extremity sensation was normal except along the anterior and outer surfaces of the ankle and foot. The anterior leg muscles were atrophied, with paresis.

Electrical excitability of the muscles of the arm and forearm was obtainable, but below this point was lost. Reaction of degeneration

was found in the muscles of the hand. The patellar tendon reflex on the right side was exaggerated. There were two or three brownish spots on the forearm, of the duration of which the patient could give no account.

Quite analogous deformities occur in the muscles of the lower extremities. The structures affected are the extensors of the toes, which are the flexors of the ankle-joint, and as a result the ankle cannot be flexed, and, in walking, the foot is raised by bending and lifting the knee-joint and the foot is carried forwards and dropped down *en masse*, or the point of the foot may trail downwards, the toes first coming in contact with the ground. There often results a condition resembling paralytic clubfoot. The toes may be flexed *en griffe*, rendering locomotion uncertain and vacillating. The atrophy may extend to the muscles of the thighs and buttocks, producing a condition resembling progressive muscular atrophy.

The muscular atrophy is characteristically displayed in the regions supplied by certain cranial nerves. It involves the trifacial as well as the facial, and the resulting deformities may resemble other facial paralyses of peripheral origin. The paralysis may affect the facial muscles, drawing the face to one side and constituting a characteristic deformity. Paralysis of the motor muscles of the eyes often gives a staring expression to the face, altering the entire physiognomy. The paralysis of the infraorbital branch causes atrophy of the lower lid and paralysis of the orbicularis. The upper lid overhangs the lower lid, which is everted, and the tears flow down the face, diverted by the deformity of the lid from their natural channel. The patient is unable to close the eye, and in the effort to do so continually contorts the face. The eyeballs roll upwards, while the lids remain stationary.*

When the fifth nerve is affected, the lacrymal glands become atrophied and disappear, and the secretion of tears is stopped. The eyelashes also fall out. The eyeball being insufficiently protected by its natural secretion becomes dry and inflamed, the cornea opaque, and the eye may be lost through ulceration of the cornea. The eyes are also liable to be injured by exposure to bright light, dust, and other irritants from loss of protection of the eyelashes. The loss of sensation may be so complete as to permit of operations for cataract or other affections of the eye without the use of an anæsthetic.

The buccal branches of the trifacial may also be affected, with

* In the pest house in San Francisco I observed three lepers, all brothers, in whom this particular form of paralysis was so marked that it was impossible for them to close the eyes voluntarily. At night the eyelids were strapped together with adhesive plaster.

paralysis of the buccinator muscles. The cheeks and lips are flaccid and pendulous. In severe cases the lips puff out, as in facial paralysis. In many cases one of the first signs of leprous involvement of this nerve is inability on the part of the patient to whistle, and pronunciation of labials is difficult. The paralysis of the lower lip causes the lip to hang down, displaying the teeth and gums, and there is a more or less continuous flow of saliva from the mouth.

The Mucous Membranes.

The trophic changes are not confined to the skin and muscles of the face, but affect also the mucous membranes of this region. The oculopalpebral membranes are subject to constant irritation from exposure to various external irritants. Owing to the lack of the normal lubricating secretion, the conjunctiva becomes dry and inflamed. Photophobia is often present in a marked degree. What has been termed a condition of "cutisation" of the conjunctival mucous membrane takes place, similar to what is described in connection with changes in the mucosa of the air passages. Phlyctenular lesions with resulting ulcerations and opacities of the cornea are apt to occur. These ulcerations are as a rule superficial and are not apt to perforate the cornea and puncture the anterior chamber.

Similar trophic changes occur in the mucous membranes of the upper air passages, being probably due to degenerative changes in the branches of the trifacial. The mucous membrane of the nasal fossæ, which in the early stage is the seat of irritation and hypersecretion, becomes dry, red, and inflamed and later the seat of ulcerative changes. The ulcerations, at first superficial, become covered with crusts which partially close the passages, interfere with respiration, and modify the character of the voice. Upon detaching or blowing out the crusts, they are found to be blood-stained upon their attached surface, and epistaxis, more or less profuse, frequently follows. The ulcerations upon the septum not infrequently lead to perforation and sometimes complete destruction of the support of the nose, which consequently becomes flattened out.

One of the characteristic mucous-membrane symptoms consists of complete loss of sensibility about the soft palate, uvula, and back of the pharynx, not amounting to paralysis, but seriously interfering with the proper function of the muscles of the throat which are affected by it. There may be regurgitation through the nostrils, causing much difficulty in swallowing. The anæsthesia is so marked that the patients do not wince when a sharp instrument is plunged deeply into the parts mentioned.

Stage of Mutilations.

Mutilations of the Skin, Bones, and Articulations.

In many cases the muscular atrophies and contractures mark the end or culmination of the deforming process. In other cases, when there is a complete disorganization of the trophic nerves, profound nutritional changes, with destruction of the bones and mutilations of the extremities, follow.

Fig. 10.—Showing the Different Stages of Mutilation in Anæsthetic Leprosy.

In the milder class of cases the trophic disorder is expressed in superficial ulcerations due to the diminished vitality of the skin from changes in its structure and the loss of resisting-power conferred by a normal nerve supply. Owing to the destruction of the sebaceous and sweat glands and the suppression of the sweat and oily exudations the skin loses its soft, supple feel and becomes dry, harsh, and parchment-like; the epidermis cracks easily and loses its protective power of shielding the underlying tissues. It has become more vulnerable to slight causes of injury.

These nutritional changes are at first confined to the anæsthetic patches, but later become manifest over the general surface of the extremities. On account of the anæsthesia wounds, burns, and various traumatisms occur without the patient's knowledge, followed by superficial ulcerations which are long in healing. Even at an early stage of the

disease the hands and feet may be covered with wounds and scars from various causes. The slightest injury may cause disorganization of the tissues. The chafing of the shoe, for example, may cause a blister with superficial ulceration which may require months for its healing. Often the skin over the joints of the hands or fingers, which are at first more prominent from atrophy of the overlying tissues, becomes thinned, cracked, and fissured, producing dry, deep rhagades, which may ulcerate and show no tendency to heal. A breach of continuity may occur in the skin over the osseous prominences of the semiflexed phalanges, the thumb, wrist, elbow, knee, metatarsal or phalangeal articulations.

The more profound trophic changes which occasion the characteristic mutilations of this form may be consecutive to caries and ulcerations of the bone, or they may take place by a process of interstitial absorption or what may be termed spontaneous resorption without intervention of the ulcerative process. In other cases the deep ulcerations may begin in the pemphigus blebs located on the phalangeal articulations, uncovering the deeper tissues, the consecutive disease of which leads to the elimination of bone and the extensive mutilations which characterize this period of leprosy.

The indolent anæsthetic ulceration which starts in the fissures of the skin, instead of remaining superficial, may become more profound and destructive. Not infrequently the parts anterior to the fissure become gangrenous, resulting in their spontaneous amputation. The reparative process is usually prompt and complete, the stump healing perfectly. At other times the ulcerative process gains in depth, destroying the cellular tissue, denuding the extremities to the bones, penetrating the articulations, and leading to loss of the bones. These ulcers, with callous borders formed by the muscular wall, are often atonic and may persist for months without healing.

In another class of cases the first sign of beginning necrosis of the bones is manifest in the swollen, tense condition of the overlying tissues and is often attended with fever and constitutional reaction. This swelling becomes softer, suppurates, and makes its way to the surface, which opens and gives exit to a collection of sanguineous pus, and there will be found a sinus leading down to the necrosed bone. This is gradually broken down and extruded by the suppurative process, when the sinus heals. In the case illustrated in Fig. 11 the entire hand was necrosed and gradually detached from the body; in the same way an entire foot may be amputated.

The following cases which came under the observation of Dr. McDougal, of New Lexington, Ohio, and were reported by him in 1895, are of exceeding interest on account of their mysterious origin.

That they are examples of leprosy there can be but little doubt, although the source of the infection cannot be definitely traced. Possibly the father may have contracted the disease in the South during his military service and communicated it to his daughters. The cases

Fig. 11.—Spontaneous Amputation of the Hand in Anæsthetic Leprosy.

are also of interest in connection with the differential diagnosis of leprosy and syringomyelia. They were diagnosticated by a number of dermatologists as syringomyelia of the Morvan type.

"Hannah M. Garey, 18 years old, first came under my observation in December, 1894. She presented the following manifestations of a disease we diagnosed as anæsthetic leprosy: The left hand and lower forearm were swollen and rather firmly thickened, the hand and wrist being about twice the normal size. The distal phalanges were all lost, except from the little finger and thumb, and the stumps

were all healed. The thumb nail was deformed and discolored. The hand was being amputated at the radiocarpal articulation by a narrow, encircling ulcerative process, and the work was so near completion that only the ulnar vessels and some of the tendons remained. Both surfaces were covered by granulations, were bathed with extremely foul-smelling pus, and were yet held in close apposition, except at the bordering skin, where some retraction had taken place in the healing process which had begun.

"The right hand and fingers were somewhat swollen and clubbed, and all the distal phalanges, except those of the little finger and thumb, were lost. The wrist-joint was somewhat deformed because of an unnatural prominence of the head of the ulna on the dorsal side. Both feet were swollen and thickened, and this condition also involved to some extent the legs, being more marked in the left. From the left foot the first and second toes were entirely lost, the third toe was off at the proximal phalangeal joint, and the fifth toe was all lost. On the plantar surface of the stump of the great toe was a thick, dark crust covering an unhealed ulcer. In the middle of the left sole was an ulcer, the size of a silver half-dollar, which reached deep into the foot and from which there came a very offensive discharge. From the right foot the great toe was lost, the second and third were off at middle of proximal phalanx, and the fourth was pointed upwards so that it was considerably out of line with the others. The little toe was not affected, except that it was involved in the general thickening of the foot. All the affected members were more or less anæsthetic, the thermal anæsthesia being especially marked.

"There was a blister the size of a silver quarter on the back of right arm just above the olecranon. The end of the tongue had been destroyed by ulcerations that had healed, the left side of the lower lip and both wings of the nose had suffered loss from the same cause and were consequently deformed, and the lower jaw had likewise suffered loss of bone, teeth, and gum. The girl's eyes looked weak and blinking, and her vision was poor.

"This malady began to manifest itself, so the mother states, by abscess formations in the legs when the patient was about fifteen months old. In two or three years the toes began to ulcerate and come off, and then the hands became involved. The flesh ulcerated from the fingers, leaving the blackened, dry bones exposed, and these she persistently drummed on the tables and chairs until her mother cut them off with shears.

"She menstruated, though irregularly, after she was fourteen years of age until about one year ago, when the menses ceased.

"January 18th, 1895, I saw her again. At that time she was sweating freely, though the house was cold, and her pulse was accelerated. She complained of pain in the neck and left leg, from which she had been suffering much. Her mother said she had lately fallen several times, limp and motionless, and that she had been having some sort of choking spells. The hand was still further separated, so that it hung downwards when the arm was raised. On the back of the hand was an extensive gangrenous blister, due to the pressure of splints used to hold the hand in position. The epidermis covering the remainder of

the hand had been recently shed and replaced by the formation of new. The blister on the elbow had healed and the skin marking its location was papery and harsh, and completely insentient to touch or pain. The plantar ulcer was healing and covered by a thick, black, offensive crust.

"February 15th I next saw her. At this time there was a large ulcer, with sharply defined edge, on the back of the hand, corresponding in size and location to the blister seen on a former visit. Since my previous visit there had appeared for the first time in the history of the case—so far as I was able to learn—an eruption on the left side of the neck and on the front of the left leg. The eruptive spots were not raised, were dark yellowish-brown in color on the leg and darker on the neck. They were thickly set, and made with the surrounding skin a dappled appearance, which shows fairly well on the leg in the photograph. Since the appearance of the eruption there have been no choking or fainting spells. The plantar ulcer, after a duration of about five years, was now healed. At this time the negatives were obtained from which the photograph was made (Fig. 11) and the hand was removed and sent away for bacteriological examination.

"Sections from this specimen were stained for lepra bacilli with negative results. The sections containing giant cells were also stained for tubercle bacilli; none were found.

"Her younger sister Hattie, eight years of age, has been afflicted for about three years. Her feet are clubbed and legs stocky. The great toe of the left foot is off at the middle of the proximal phalanx. There is a dark crust on the lower part of the stump. The distal phalanx of the second toe is lost. The right great toe is like the left. The nail is lost from the second toe, and the ulcer which was present on the top of this toe is now healed. The little toe has been entirely destroyed and a healthy stump remains. There is some anæsthesia of the feet and legs. There was a moderately indurated swelling on the outer front side of the leg just above the ankle, which has almost disappeared.

"The hands are also affected. They are thickened and chubby. The thumb nails show evidence of disease. The ends of the index-fingers are off, and here an apology for nails is offered in the existence of small, dark, horny thickenings on the centres of the ends of the fingers. On the radial side of the wrist the skin is rough, and here are a number of small wart-like elevations. There are a number of blisters on the palmar surfaces of the hands. These are accounted for by the fact that she is fond of parching corn in a skillet on the stove, and her touch cannot appreciate a destructive degree of heat; consequently her hands are frequently burned. She is unable to appreciate any difference between the feel of a bottle filled with hot and another filled with cold water. Her eyes are red and tearful. Her voice is coarse and croaks, and she has a croupy cough at night.

"Both have suffered at times from painful nerves, and when deep abscesses formed, or when amputations began in the bones, they suffered from them. But the ulcerations, though reaching deep into the tissues or even destroying a member, have not been painful.

"Hannah walked with little discomfort on the plantar ulcer, and during the later stages of the destructive process that robbed her of her hand she suffered none, and laughed when it was being cut away.

"The mother insists that the ulcerations are always the result of some accidental injury. They sometimes heal kindly after a variable duration, and sometimes go on to complete destruction of the part."

In a recent communication (May 12th, 1899) Dr. McDougall states: "Hannah continued losing remnants of her fingers and toes and having plantar ulcers until she died from pneumonia this spring. The living girl has suffered some further mutilation of the feet since I last saw her. The first, second, and fifth toes are now gone from the left foot. There is also a deep ulcer in the plantar surface at the middle of the heel. It is indolent, dark, and deep, and rather dry so one can see into it. It would admit a lead pencil nearly an inch. The mother says it came a number of weeks ago from stepping on a nail. The foot is also swollen and inflamed from the formation of an abscess which has opened through a round hole in the top of the foot an inch from the base of the second toe. The discharge is thin, purulent, and offensive. Notwithstanding the condition of the foot she walks and runs with no sign of pain except a moderate limp. The mother says the gathering was caused by the 'mare' stepping on the foot. Thermal anæsthesia seems complete about the external malleoli and for a little way above. We filled a two-ounce bottle with hot water and one with cold, and grasping them with her hands, she could not distinguish them. There is quite marked thickening of the left ulnar nerve."

FIG. 12.—Spontaneous Amputation of the Toes in Anæsthetic Leprosy.

These sisters have never been outside the State of Ohio. Both parents and all the grandparents were natives of Ohio, and belonged to healthy, long-lived families. The parents were married in 1866. There are eight children, and all are healthy except Hannah, the fourth born, and Hattie, the last born. The mother is forty-four years old and healthy. The father, who was a soldier during the War of the Rebellion, is reported as having died of some brain trouble March 10th, 1893. He had an offensive discharge from the nose and an eruption on the upper lip and the end of the nose. This trouble developed shortly after marriage, and was never recovered from. The regiment of which he was a member was stationed, during the few months it was in service, at Nashville, Tenn., and at Dalton, Kingston, and Macon, Ga.

Perforating Ulcer.—The plantar ulcer which is so common and characteristic a symptom of this form of leprosy is only a deep-seated necrosis due to trophic disorders, the starting-point of which may be an injury of the integument. It occurs most frequently among lepers

who go barefoot, and is often due to a stone bruise or other injury. It usually begins as a circumscribed callosity which appears over the sole of the foot or palm of the hand or upon any portion of the metatarsus or metacarpus. It rarely affects the phalanges or bones which are easily detached, but more often bones which are firmly impacted and cannot readily be dislodged. The epidermal thickening is usually uplifted in the form of a bleb or blister and gradually breaks and becomes ulcerated. The ulcer increases in depth until it finally reaches the bones, which it slowly disintegrates and destroys. These ulcers are essentially atonic and may persist for months and years with but little change. It has been found that if a necrosed bone is cut down upon and removed the ulcer heals. These perforating ulcers

Fig. 13.—Plantar Ulcer.

lead to various mutilations and often necessitate the amputation of the member. In other cases the lesion can scarcely be described as an ulcer, but rather as a sinus leading from an aperture in the centre of the callosity down to the necrosed bone. The walls of the sinus are lined with fungoid granulations, which may be found protruding from the opening. Around the granulations is found a flattened area of whitish-yellow, thickened epidermis.

Spontaneous Resorption of Bones.—In another class of cases the disappearance of the bones is a phenomenon of absorption. It has been described as a species of rarefying ostitis, giving rise to what may be fitly termed leprous osteomalacia (Leloir). It is more apt to affect the contracted fingers in cases of *main en griffe*. The phalanges, or the bones of the metacarpus and metatarsus, gradually atrophy and melt away until only the fibrous tissue which formerly enclosed them remains. This also shrivels up and becomes mummified until the fingers may be no thicker than a pencil. The process usually first attacks the second phalanx. One phalanx after another may be removed in the manner described until the phalanges of the fingers and toes

are all destroyed. It may affect one phalanx and respect the others. Thus the second phalanx may be destroyed, leaving the first and third intact; or the second or third may be destroyed, and the first may rest upon the metacarpus.

The nail seems to be endowed with a remarkable power of resistance. As one bone after another is destroyed the fingers shrink and shrivel up until nothing may be found except the nail occupying the metacarpal or metatarsal bone corresponding to the phalanx. In rare cases the terminal portion of the phalanx may be encircled by a fissure which gradually deepens until the constricted portion in front becomes swollen to twice or three times its normal size and is attached only by a narrow pedicle suggesting a similitude to certain cases of ainhum. Although the nails are seen to be endowed with a wonderful resistance even at an advanced stage of the disease, they may suffer in their nutrition. The dystrophic changes are seen in thinning of the nail and more or less complete exfoliation, with degeneration of the matrix. In some cases the end of the finger is seen capped with a slight rudimentary vestige of a nail.

The mutilations of leprosy which represent the profoundest grade of leprous destruction may in some cases coexist with a condition of comparative health. The patient may live for many years in this stunted and maimed condition, although practically helpless. Ordinarily in the advanced stage of the disease there develop certain constitutional disorders. Morbid stomachal conditions lead to emaciation and the general health gradually fails, with a tendency to visceral complications.

Patients complain of sensations of chilliness and cold. This form of subjective sensations constitutes one of the most constant and distressing symptoms. Patients hug the stove or fire in their ineffectual efforts to keep warm, and to this is often due the frequent occurrence of burns among lepers.*

Hillis, as well as Daniellsen and Boeck, have observed that the body temperature is several degrees below normal in the advanced stages of the disease. Coincident with the subnormal temperature the action of the heart is enfeebled, and there is diminution in the frequency of the pulse.

Sexual Functions.—The inhibitory effect upon sexual desire and capacity is less marked in nerve leprosy than in the tubercular form. In many cases it would appear that this function is at first stimulated and the extinguishment of sexual desire and capacity takes place

* A similar phenomenon is observed in morphœa of generalized distribution. In such a case under my observation the patient would sit for hours in the sun enveloped in a blanket or close to a fire in a vain endeavor to keep warm.

more gradually and at a more advanced stage of the disease. I may quote from a letter of Mr. Dutton, who has charge of the Home for Leper Boys in Molokai, as to the effect of the two forms of disease upon sexual functions. "Notwithstanding the old belief that in the tubercular form this function assumed unusual excitability, it has always seemed to me that this condition lay with anæsthetic cases, or with the mixed cases. Of home inmates who leave the home to live with women, I should say that they are generally those who have marked anæsthetic features." This result is precisely what would be inferred from the implication of the testicles by the bacilli in the tubercular form, and the comparative exemption of these organs in the anæsthetic form. It has been demonstrated by Babes and others that the bacilli are found in great abundance and are localized in the connective tissues and seminiferous tubules in the tubercular form.

The procreative capacity of lepers is not so much impaired as is commonly believed. The statistics of the leper settlement of Cape Town, and of the Norwegian lepers who have emigrated to this country, to which reference is elsewhere made, show that lepers may be quite prolific.

Menstruation.—In most cases, especially if the disease has existed for some time, the menses become irregular, and in exceptional cases they cease completely long before the normal period of the menopause. When leprosy develops in childhood or before puberty the menses rarely appear at all. The disease has an inhibitory effect on this function, as well as a stunting effect upon the growth, arresting the development of the normal bodily functions. The aspect of precocious senility, the nervous trouble culminating in contractures, ulcerations, and consecutive mutilations with progressive emaciation, form an easily recognized picture of leprosy in childhood.

Termination.

The lamentable aspect presented by trophoneurotic lepers at an advanced stage of the disease has been thus graphically described by Leloir:

"The anæsthesia may occupy the entire body. In any case it has invaded the upper and lower limbs completely, the face, etc. The facial mask is immobilized by paralysis and muscular atrophy, and in this yellowish, waxy, cadaveric, emaciated and deformed immobile mask one sees two large eyes, open, fixed, but white, dull, without light, for the unfortunate is blind. Saliva constantly flows from the corners of the paralyzed mouth. The nose is sometimes deformed; the sense of smell has disappeared partially or altogether, likewise the taste; the hairs of the face have fallen.

"The hands and feet are horribly deformed and mutilated, and have no longer a human appearance. The muscles of the limbs are atrophied. Ulcerations, more or less vast, have denuded the bones of the limbs and secrete an indescribable humor. The patient exhales a sweet, unsavory odor analogous to that of the warm cadaver. He is in a state of profound depression; deprived of appetite, tormented by insatiable thirst, sometimes again by frightful neuralgic pains; he remains lying or sitting entire days, without occupying himself with that which is passing around him. One is obliged to feed him, put him to bed, carry him. He appears plunged in a profound stupor and witnesses indifferently the progressive mutilation of his body. Neverthless, if one interrogates him, one perceives that his intelligence is rather dulled than lost."

Patients die of marasmus or exhaustion consequent upon long-continued digestive disorders, colliquative diarrhœa, of amyloid degeneration of the kidneys and internal organs, or of some intercurrent disease. They rarely die of tuberculous complications. Such complications are as uncommon in this form of leprosy as is amyloid degeneration in the tubercular form.

The average duration of life in the anæsthetic form is said, by Daniellsen and Boeck, to be from eighteen to twenty years. In some cases this period is prolonged to twenty, thirty, or forty years or longer. The transition of the anæsthetic into the tubercular form will be considered in connection with the mixed type of leprosy.

Instead of proceeding to this fatal termination, anæsthetic leprosy, after attaining a certain degree of development, may be apparently arrested. All the symptoms abate, the spots gradually clear up, the bullæ cease to appear, even the sensibility of the skin, which was in abeyance for a long time, becomes reëstablished. While the patient may show in his atrophied and paralyzed muscles, his maimed and mutilated limbs, the vestiges of the disease which has occasioned them, there is no evidence that the bacilli are present or likely to be awakened into activity. The patient may live to quite an advanced age, and finally die of intercurrent disease.

This arrest may take place at any time during the course of the disease, and it is a question of great practical importance whether such cases can be considered cured. Impey says that in every leper establishment there may be found cases of cured leprosy. In his opinion these stigmata of the disease have the same significance as the scars of syphilis, and as a practical outcome of this belief he insists that it is wrong to confine such cured cases in close association with tubercular lepers as they are liable to be reinfected. A number of cases are instanced in which he thinks reinfection has taken place,

the patient again exhibiting the early and late phenomena of the disease precisely as if he had never had it. To this Ashmead replies: "How can immune tissue be inoculated? Certainly the anæsthetic leper would be more liable to be contaminated in his healthy parts by autoinfection than by other lepers. If the cutaneous tissues of the anæsthetic leper are immune, how can they be inoculated at all?" To this it may be replied that it is quite possible that the few bacilli in an old case of nerve leprosy may have lost their infective capacity, while a plentiful supply of bacilli from a fresh source and of a more virulent type might inoculate previously immune tissues.

Personally, the writer believes that there are a great many cases of anæsthetic leprosy which are abortive or which are spontaneously cured. On the other hand it is to be borne in mind that anæsthetic leprosy, instead of running a distinct course to the end, may take on the severer and more rapidly fatal characteristics of tubercular leprosy. Fortunately, the transformation of the milder anæsthetic form into the severer tubercular is comparatively rare.

Tubercular and Anæsthetic Leprosy Contrasted.

In order to bring into strong relief the clinical contrasts between tubercular and anæsthetic leprosy, the more distinctive characters of each may be thus formulated:

Tubercular Leprosy.	Anæsthetic Leprosy.
Bacilli	*Bacilli*
Abundant; found in the cutaneous and mucous-membrane lesions, physiological secretions, inguinal glands, and the internal organs.	Comparatively few; found in nerves and sheaths, sparingly and not constantly in cutaneous and mucous-membrane lesions.
Mode of Infection	*Mode of Infection.*
Unknown, probably multiple.	Unknown, probably multiple.
Period of Incubation.	*Period of Incubation.*
From several months to few years.	Months and years, relatively longer.
Prodromes.	*Prodromes.*
Fever, malaise, epistaxis, systemic disturbance.	More localized, hyperæsthesia, neuralgic pains, and other sensory disorders.
Early Eruptive Stage.	*Early Eruptive Stage.*
Erythematous and pigmented spots, circular in outline, reddish in color, which is more pronounced in the centre, fading towards the circum-	Erythematous, pigmented, and achromatic spots; bullæ, spots more numerous and more irregular in shape, smaller at first, with a tendency to spread

ference; edges not raised, spots pale on pressure, transient in duration, may appear and disappear a number of times before becoming the seat of tubercular nodules; eruption more frequently appears on the anterior aspect of the body.

Tubercular Stage.

Development of tubercles in skin and mucous membranes, which may come out in successive crops, remain permanently or disappear by interstitial resorption, undergo fibroid degeneration, or become ulcerative.

Ulcerative Stage

Softening and breaking down of tubercles, disappearance by purulent dissolution or by resorption; lepromatous infiltrations of internal organs.

Mucous Membranes.

Seat of diffused and nodular infiltrations followed by ulceration; mucosa of eye, nose, pharynx, larynx, seat of nodular infiltrations followed by ulceration.

Secretory Glands.

Sebaceous and sweat secretions, first exaggerated, later diminished.

Hair Follicles.

Loss of eyebrows, alopecia of all pilous surfaces the seat of tubercular infiltration.

Nails.

Often affected by tuberculous infiltrations of matrix or ungual borders, followed by ulceration, simulating syphilitic onychia and paronychia.

Sensory Disorders.

Disorders of sensation not so marked; anæsthesia, if present, is usually localized, limited to the tubercles or surrounding regions; probably due

peripherally and serpiginously and form by coalescence large patches which are white and depressed in the centre, with raised, well-defined hyperchromatic borders. These patches are permanent, and remain as long as the disease lasts. They are more numerous on the back than on the front of the body.

Atrophic Stage.

Muscular atrophies, tendinous retractions, deformities, paralyses, with sensory disorders, anæsthesia, etc.

Mutilating Stage.

Osseous degeneration, loss of members by resorption of bone, ulceration, gangrene, perforating ulcer, etc.

Mucous Membranes.

Mucous membranes not so frequently affected; changes not neoplastic, but essentially dystrophic; eye, nose, pharynx, and larynx more frequently exempt.

Secretory Glands.

Primary exaggeration of function with secondary atrophy and suppression of function.

Hair Follicles.

Loss of eyelashes, bleaching and falling out of hairs from atrophy of the follicles.

Nails.

Changes chiefly atrophic, the nails preserve their autonomy in most surprising manner.

Sensory Disorders.

Hyperæsthesia, pruritus, and pain pronounced during the early irritative stage, succeeded by numbness and anæsthesia, more pronounced in mac-

to pressure upon the terminal filaments of the nerves by leprous infiltration.	ular patches, but may affect surface of entire limbs; disassociation of modes of sensation, due to more or less complete degeneration of the peripheral nerves.
Sexual Functions.	*Sexual Functions.*
Sexual desire and capacity soon lost; impotence from azoospermia.	Sexual desire at first exaggerated, suggesting satyriasis; sexual capacity continued longer.
Inguinal Glands.	*Inguinal Glands.*
Changes constant and characteristic; thought to constitute centres of autoinfection.	Enlargement of glands exceptional, not probably due to leprous virus.
Internal Viscera.	*Internal Viscera.*
Seats of leprous infiltration as well as of tuberculous and other terminal infections.	Amyloid degeneration more common.
Course and Duration.	*Course and Duration.*
Disease more severe, more rapidly progressing to fatal termination. Average duration, eight to ten years.	Disease milder, less progressively active; duration indefinite, fifteen to twenty years or longer.
Termination.	*Termination.*
Tuberculous complications, exhaustion from leprous ulcerations, nephritis, colliquative diarrhœa, septic infections; suffocation from atresia of air passages.	Amyloid degeneration of internal organs, albuminuric nephritis, rarely phthisis.

It may be observed that while the clinical pictures of the two principal forms of leprosy present many features of difference in their fully developed stage, the lines of demarcation between them are not always so clear or sharply drawn as would appear from the above differential table.

Certainly during the invasion period the prodromal symptoms are not sufficiently distinctive to enable us to forecast the form the disease will eventually assume. With the advent of the eruptive stage the divergence between the two forms becomes more marked. But even when we recognize a predominance of the tegumentary lesions on the one hand or the marked implication of the nervous system on the other we cannot say that there will be a fixation of one form or the other.

In order to bring the distinctive differences of the two forms of leprosy into more prominent relief a typical picture of each form, one beside the other, may be seen in Fig. 14. In one it is to be observed that the visage is covered with nodular masses, marked by

deep corrugations, the lobes of the ears are enlarged, flabby, and pendulous, but the integrity of the extremities is completely preserved; in the other the bridge of the nose is sunken from osseous

Fig. 14.—Contrast between Tubercular and Anæsthetic Leprosy, as Exhibited in the Face, Hands, and Feet.

absorption, the features are drawn by facial paralysis, the fingers are distorted and mutilated, and the feet are mere stumps, with partial vestiges of the toes remaining.

But to demonstrate the substantial identity of the two forms, a picture of mixed leprosy is shown in Fig. 15, in which may be observed, in addition to the mutilating changes in the nose, hands, and feet, tubercles on the cheek and ear. This case was primarily anæsthetic, but after a certain time tubercular changes supervened.

FIG. 15.—Mixed Leprosy, Primarily of the Anæsthetic Type with Tubercular Changes Supervening.

Mixed or Complete Type of Leprosy.

Under this designation are included certain cases in which the characteristic lesions of both the tubercular and anæsthetic forms appear either simultaneously or successively.

(1) Symptoms peculiar to both forms may be present from the first in consequence of simultaneous invasion by the bacilli of the cutaneous and nerve tissues, the course of the disease being influenced favorably or unfavorably according to the predominance of the nerve or cutaneous lesions.

(2) The bacilli may first attack the peripheral nerves and the initial symptoms be those of anæsthetic leprosy. After the disease has run a certain course it may become complicated by the development of tubercles and correspondingly intensified in severity from the invasion of the integument by the bacilli.

(3) The leprous virus may first affect the skin and mucous membranes with the production of tubercles and other changes peculiar to the tubercular form, but in the course of its evolution the bacilli leave the integument and invade the peripheral nerves. The disease then exhibits the milder symptoms of the anæsthetic form, which is less progressively active and the duration of life is considerably prolonged.

According to Leloir there may be a coincident development of both forms, a transformation or a gradual transition of one form into the other, and also a complete substitution of one form for the other; the symptoms of one form replacing those of the other precisely as if a new infection had taken place. In the latter case it is assumed that the bacilli, having exhausted the tissue soil in which they first find lodgment, invade new tissues which were previously immune.

It is probable that in all of the cases of reputed transformation or substitution, the symptoms of both forms may have coexisted without recognition, the manifestations of the predominant form masking those of the other.

The lines of demarcation between tubercular and anæsthetic leprosy are not so distinct and sharply drawn as to enable us to separate and classify them on the basis of their pathogenic mode. The intimate sympathy existing between the cutaneous and nervous systems in their nervous and nutritive relations explains the similarity in the morbid phenomena exhibited by each; the more especially as these phenomena are due to the same pathogenic factor.

The proportion of mixed cases varies in different countries. In

Norway the proportion of nervous leprosy was 33.3 per cent., mixed leprosy 15.1 per cent., tubercular leprosy 51.6 per cent. In 188 cases in British Guinea tabulated by Hillis there were found 34 cases of tubercular, 51 of mixed, and 103 cases of nerve leprosy. In India Carter's tables of the relative frequency of the different forms show that 9 per cent. were tubercular, 21 mixed, and 61.9 anæsthetic. Impey's tables show that of 703 patients admitted into the Robben Island Asylum, Cape Colony, South Africa, there were 369 anæsthetic cases, 238 tubercular cases, 81 mixed, and 15 syphilitic, making a percentage of 52.48 anæsthetic, 33.86 tubercular, 11.53 mixed, and 2.13 syphilitic cases.

Taking the observation of ten hundred and fifty cases which I saw in the Molokai settlement in 1889 as a basis of calculation, it may be roughly computed that one-half were tubercular, one-third anæsthetic, and the remaining one-sixth of the mixed type. Since then the relative proportion of anæsthetic and mixed cases has largely increased.

The Survival of Leprosy in Modified Forms.

It is generally accepted that leprosy practically disappeared from Europe during the fifteenth and sixteenth centuries, and that within the last two or three centuries cases of this disease met with in central Europe have been imported cases. Nevertheless, it has been contended by certain authors of more or less note that certain rare forms of disease occasionally met with in leprosy-free countries, and which have been classed as distinct morbid entities, represent survivals of leprosy.

Erasmus Wilson, the distinguished English dermatologist, in his text-book on skin diseases (1865), discusses the question whether the leprosy of the Middle Ages is gone and left no remains behind. "Are there no traces of the great leprosy at the present day?" To this he answers: "It would be contrary to all analogy to suppose that it has so totally passed away as not to leave a trace; and yet no sign exists in the records of medicine to tell us that such is not the case. But although the sign may be absent in the records of medicine, the infallible sign remains imprinted on man. Leprosy remains among us still, but only as a faint trace of a worn-out disease or as an ember of the burnt-out fire. God forbid that the spark should be rekindled! I repeat that elephantiasis still exists among us in this country as a *faint trace* of its former self, and the observation of that trace, however faint, becomes a matter of interesting search. Although a mere shadow in comparison with the parent disease, it is nevertheless sufficient to occasion considerable annoyance to the sufferer and to bring him not unfrequently under the inspection of the medical

man. Now when once pointed out can the medical man doubt or an instant the nature of the disease which he has before him? There is the insensibility, the deposition, the blanching, the exhaustion of function, and the atrophy of the parent malady with all their original distinctness; indeed, one complete symptom of the pure elephantiasis preserved unchanged as it existed among the Jews and as it is to be found at this moment on the shores of Norway, the symptom which was called by the ancients morphœa."

He declares that the various forms of morphœa which he describes under the definition of morphœa alba ladarcea, morphœa alba atrophica, and morphœa nigra are remains of that bygone scourge, the great leprosy. He also declares that alopecia areata is a morphœa of the scalp and the hair-bearing skin, and that this morphœa bears the same relation to elephantiasis as the morphœa already described.

Kaposi also includes the different varieties of morphœa in his description of the macular form of leprosy. He states that the several forms of this spotted or macular leprosy may exist alone for years as the chief signs of the disease and constitute two different types. "Thus, for instance, (*a*) they may exist as such for years, or either terminate as such without ever undergoing any further alteration. To a certain extent they represent local forms of lepra, since during their entire period of existence, as well as after they have passed away, the system does not become in the least affected by them. Or (*b*) they may last for a long time uncomplicated; but sooner or later the whole system becomes affected, and the series of symptoms characteristic of anæsthetic lepra make their appearance, among which the symptoms of maculated lepra occupy only a subordinate place."

At the present day the most prominent advocate of the survival of leprosy in Europe and elsewhere under the form of rare diseases is Zambaco Pacha. In his paper before the Berlin Leprosy Congress he has endeavored to widen the pathological field of leprosy by bringing within its domain syringomyelia, Morvan's disease, scleroderma, sclerodactylia, Raynaud's disease, morphœa, ainhum, and progressive muscular atrophy of the Aran-Duchenne type.

He claims that in Europe, and in countries where leprosy has ceased to exist as an endemic, it still survives in a degraded form, and that the above-mentioned diseases constitute attenuated or abortive types of leprosy; in other words, they represent a leprosy "*larvée*," modified and attenuated in its manifestations. He asserts that the universal belief that leprosy has disappeared for two centuries from Central Europe and the non-recognition of the numerous varieties of this disease which have been modified by the progress of civi-

lization have contributed to engender errors, and that these surviving forms of leprosy have been designated under the title of cases of rare, nameless, and undescribed forms of disease. While their resemblance to leprosy has attracted the attention of many distinguished observers, all have refused to recognize the true nature of these diseases upon the ground that they cannot be leprosy, since this affection does not exist in Europe, and that the patient has not been in any leprous locality where he could have contracted the disease.

Zambaco declares that Morvan's disease is nothing less than leprosy, and that syringomyelia and Morvan's disease constitute one and the same thing. He thinks that there have been confounded under the title of syringomyelia numerous cases of leprosy exhibiting the anæsthetic form of the disease. Progressive muscular atrophy of the Aran-Duchenne type embraces also different diseases, among which figures leprosy. Raynaud's disease and symmetrical gangrene depending upon nervous troubles, circulatory and trophic, present the closest relations with certain forms of leprosy. He declares that one may place with certainty among them many cases of leprosy. He thinks it probable that future research will demonstrate that they are no more than new morbid states of a leprosy modified and attenuated in its manifestations. The ainhum of authors, when affecting the hands or feet is, according to Zambaco, a form of mutilating leprosy. The morphœa of modern writers and the morphœa of ancient writers should not be separated from classical leprosy. Scleroderma and sclerodactylie seem to him to be only a modified leprosy, if not an unmistakable leprosy as one sees in so many of the published cases. All of these diseases he regards as more or less degenerated forms of the ancient leprosy, and he endeavors to establish their identity by grouping them under the generic name of *leprose*. Although these various diseases differ in appearance, and are sometimes quite dissimilar in their extreme symptoms, yet they approach and blend in their common symptoms and permit a pathogenic unification. He takes the ground that the absence of anæsthesia and of the lepra bacillus in these diseases is not sufficient to make us reject the diagnosis of leprosy. The symptomatology of these newly created diseases is merely an expression of the polymorphism of leprosy.

It is not possible within the limits prescribed for this article to enter into an exhaustive study of the question of the identity of these diseases with leprosy. It is sufficient to say that the views of Zambaco Pacha were not shared by the great majority of the leprologists present at the Leprosy Congress.

It may be said that the above-mentioned diseases are by no means uncommon in the United States, where leprosy has never existed

except in sporadic and imported cases. The ancestry of many individuals exhibiting these diseases may be traced back several generations, and found to be free from all leprous taint, while the patients themselves have never been exposed to contact with lepers. To speak of a survival of a disease which has never existed, in this country at least, is a contradiction of terms. The assumption that these diseases are expressions of leprosy involves the theory that the leprous germs must have had their origin in a remote ancestry and remained latent for several generations and then have been transmitted in this modified form, which is stretching the theory of atavism to an impossible degree.

In commenting upon the disappearance of leprosy from Europe, Jonathan Hutchinson says "it is very important to remark that, so far as our knowledge at present goes, it has left nothing behind it. We have no half cases or slight forms or modified maladies. Its manifestations seem to be somewhat more definite and positive than those of tuberculosis. It is either leprosy or nothing. Nor are there any sporadic cases springing up here and there in communities which have long been free." The results of the recent congress at Berlin have strongly confirmed these statements. No examples were produced, with one possible exception from a town in Brittany, showing that the disease had occurred sporadically in inland communities otherwise free. But many examples were produced showing that the disease is and has been for a long time prevalent to a slight extent in localities not previously recognized as its haunts.

The most convincing argument, however, which may be adduced in refutation of the views of Zambaco Pacha is the absence in all these diseases of the lepra bacillus. It is generally recognized that the presence of Hansen's bacillus constitutes the distinctive essential anatomicopathological characteristic of leprosy. It is the pathognomonic sign, and while it is not always practicable to demonstrate its presence in nerve leprosy during life, it is always found at autopsy.

The more important differential features which distinguish these diseases from leprosy are considered in the section on Diagnosis.

PATHOGENY AND GENERAL PATHOLOGY.

Infection by the Bacillus.—As in the case of other granulomatous processes, Hansen's bacillus attacks the various cellular elements of the body and is able to penetrate readily every variety of cell. Speaking generally, the changes induced in the latter consist principally of enlargement, vacuolization, segmentation of the nucleus, disappearance of pigment. Multinuclear and giant cells are formed at times.

Homogeneous yellow masses are formed at the expense of the cellular contents, and the protoplasm of the cell may be wholly replaced by the bacilli. The latter are situated both within and between the cells. The bacilli in time show degenerative changes, and we may see side by side degenerated bacilli in apparently healthy cells and young fresh bacilli in degenerated cells; these phenomena are held to be illustrations of Metchnikoff's doctrine of phagocytosis and of the war to the death between the bacilli and cells (Babes). Of all prominent histologists, Unna alone puts forward the claim that the bacillus is entirely extracellular. Unna claims that the regular and constant seat of the lepra bacilli is extracellular, their habitat not being in the protoplasm of the cells, but in the intercellular and interfascicular spaces—the lymphatic spaces in other terms. Almost all other histologists who have investigated the matter maintain that the mass of bacilli found in sections or from scrapings of the lepromes are bacilli-bearing cells—the leprous cells of Virchow. They see one or many nuclei more or less altered and a vacuolized protoplasm containing parasites—where Unna describes a "glœa," a gelatinous or mucous substance, the product of the secretion or degeneration of the bacilli having englobed the nuclei of the cells which limit the spaces in which the "glœa" is developed. It is probable that the bacilli may be either intracellular or extracellular, may be comprised in the preformed canals in which are moulded the mass of bacilli comprised in the sheath; from this result the "globi" which have been mistaken for cells.

During its period of incubation or latency Hansen's bacillus is believed, purely from analogy, to lie within the lymph ganglia.

At the moment when the bacillus is about to attack the tissues it is agreed by most authorities that it occupies the lymph spaces and makes its first assaults upon the endothelia of these cavities. The endothelia and perithelia of the lymph and blood capillaries are, according to Babes, specially subject to attack, and the lumen of these vessels often shows the presence of the parasite. The fixed connective-tissue cells, wandering leucocytes, plasma cells, etc., are in turn attacked. Wherever the parasite begins its assaults an inflammatory focus slowly forms, consisting of round cells with a single nucleus. While the cells which lie within the focus soon take on those peculiarities of size, shape, and texture which appertain to the specific lepra cell, and which have already been indicated, there is an outlying zone of ordinary round-cell infiltration which is common to all chronic inflammation.

Tubercular Leprosy.

In this variety, which is essentially an affection of the skin and mucosa, there is present a more or less diffuse infiltration which extends to the subcutaneous or submucous tissues.

With regard to the skin, there is an obvious but ill-defined distinction between ordinary tubercular or mixed leprosy and the purely neurotic form which is accompanied by certain secondary cutaneous lesions. While some of the latter are non-specific and, as might be expected, contain no bacilli (such, for example, as the pus from a perforating ulcer of the foot), others undoubtedly do contain the parasite; this has been found in the hyperæmic areas of acute lepra, which often accompany the neurotic form and in which Philippson found bacillary emboli.

In the fresh eruption of anæsthetic leprosy bacilli have been found both in and beneath the skin and also in the cutaneous nerves, both superficial and deep. Babes believes that the bacilli are originally present in all the cutaneous lesions in nerve leprosy, but that they disappear later. Darier has studied the structure of the erythemato-pigmentary macules, the so-called "leprides," and their contained bacilli. He demonstrates a more or less abundant infiltration of cells disposed in the form of cylinders around the blood-vessels, which in certain regions may become confluent *en nappe*. These are, in the majority, small connective-tissue cells with which are mingled in variable proportions white corpuscles, plasma cells, some mastzellen, and in rare cases giant cells. In nine cases which he examined he found in all but one the presence of bacilli, whether the patches were recent or ancient, erythematous or purely pigmentary. The bacilli in some cases were scarce, in others almost innumerable. Darier claims that the almost pathognomonic structure of the macules, and the almost constant presence of the bacilli in their interior permit of an early diagnosis, which is scientifically certain.

In tubercular leprosy proper the anatomical appearances vary considerably in proportion as the deposit is recent or old. Young, fresh nodules lie somewhat removed from the epidermis, a broad stratum of normal skin intervening. The infiltration begins, as do similar granulomatous processes, about the pilosebaceous follicles, vessels, nerves, and sweat glands; and one or the other of these structures forms the centre of the future nodule. Besides these specific foci the skin in general about the latter is the seat of ordinary simple round-cell infiltration. This infiltration may be diffuse without a marked nodular disposition. Sections of recent leprous tubercles show the

layers of the epidermis perfectly preserved and normal. The papillæ are somewhat hypertrophied and filled with small round cells. In old tubercles the papillary outlines have disappeared and the entire stratum is replaced by a uniform layer of small cells. The entire dermal tissue is infiltrated with round or ovoid cells which are here and there grouped in illy defined masses and penetrate into the cellular adipose tissue. The adventitious tunics of the blood-vessels, as also their internal layers, are thickened and their calibre is narrowed. The sebaceous and sudoriparous glands are implicated and choked by the production of small cells formed at their periphery and end by atrophying and finally disappearing.

The bacilli are found not only in the blood-vessel cells, but also outside of cellular formations in the lymphatic spaces. The cells designated as "lepra cells" by Virchow are found in the dermal groups of old tubercles. These voluminous cells possess several nuclei; they are ovoid, spherical, or irregular, and sometimes as large as the giant cells of tuberculosis, with which they may be confounded. In old tubercles the epidermis is thinned, the papillary layer is effaced, and no trace of the glands or hair follicles remains.

As the nodules progress they approach nearer to the epidermis, increasing at the periphery, while degenerative changes take place in the characteristic cells and the centre becomes necrotic. The casting out of this slough leaves an ulcer. The slough is made up of degenerated cells and colonies of bacilli and is due to the action of the toxins formed by the latter. The ulcer may readily heal, or the outlying inflammatory zone may undergo the leprous transformation, so that the ulcer may increase in size and depth.

Appendages of the Skin.

Next should be considered the action of the bacillus upon the hair follicles, vessels, nerves, epidermis, and sweat glands.

The bacillus appears to have a special predilection to settle about the hair follicles, and perifollicular foci of disease result, with extension of the process through the wall of the follicle. The bacilli are also encountered in the hair papillæ, and hair formation is arrested, causing the loss of hair on the surface of the body and especially the falling of the eyebrows. The bacilli are also found in the sebaceous glands which communicate by their excretory ducts with the hair follicles. It results from this disposition that the bacilli situated in the sebaceous glands, in the hair papillæ, and in the sheath of the follicle may migrate along the follicle and thereby reach the free surface of the skin. It is possible that they may penetrate the skin from the

outside by the same channels. The follicle is very little altered by the disease, but its epithelia show slight proliferation, which accords with the action of the bacilli upon other epithelial tissue. The bacilli are not invariably found in the hair follicles or the sebaceous glands in connection with them; Cornil and Babes, indeed, say that they are encountered there but rarely. With regard to the sebaceous glands in general, the epithelia at first proliferate, but the glands are ultimately destroyed. Bacilli are not found in the interior of the sudoriparous glands.

Aside from the phenomena of essential nerve leprosy, the terminal nerve fibres within the skin, being an integral part of the latter, undergo special alterations during the general infiltration of tubercular leprosy. These terminal nerves are, like the hair follicles, predilection tissues of the bacillus. Both afferent and efferent nerves and Pacinian corpuscles are attacked and at times undergo remarkable changes, the smallest fibres becoming thick cellular cords, and all these structures show an invasion of bacilli with new formation of connective tissue and blood-vessels and degeneration of the essential nerve substance with occasional regeneration. In mixed leprosy these phenomena are associated with secondary changes in the terminal nerves due to disease of the parent trunk.

When the bacilli reach the epidermis and attack it directly, we have, according to Babes, proliferation of the keratogenous cells alone or of the mucopapillary layer. In the former case leprous tylosis results, and in the latter leprous warts develop.

Still more remarkable is the action of the bacillus upon the sweat glands. Side by side with proliferation of the interstitial connective-tissue stroma of the gland we see new formation of the glandular epithelia, and we are therefore justified in speaking of leprous adenoma or adenoleproma. The fact that the bacillus is able to cause proliferation of all epithelial tissues, as well as of the fibrous tissues, seems to justify the claim that the action of the bacillus in a leper may be sufficient to cause epithelioma, which is occasionally observed.

It is thus seen that, while the maximum intensity of the toxins tends to cause destructive lesions through terminal necrosis of the infiltration leading to ulceration, every variety of constructive lesion may coexist, due to proliferation of most of the anatomical elements of the skin. Further, some of the destructive lesions undergo partial repair (cicatrization of ulcers, sclerotic changes, regeneration of nerves), and when we add trophic alterations due to disease of the nerve trunks and centres and the results of the action of associated microorganisms (pyogenic cocci, etc.) it becomes evident that the pathology of cutaneous leprosy is extraordinarily complex.

The Mucous Membranes.

Following the law that the parts most frequently affected are also earliest affected, we must regard the nasal and laryngeal mucosæ as specially predisposed to leprosy. The structures about the fauces possess more immunity, and the posterior wall of the pharynx most of all.

Leprous changes are most characteristically seen in the nasal mucous membranes, and the pathological alterations in these now to be described will apply, with certain modifications due to peculiarities of anatomical structure, to the mucosa of the upper air passages.

Leprosy in this locality is characterized not only by its early and almost constant appearance, but by its very rapid course, which leads to destructive lesions at a stage when alterations of other tissues of the body are in their formative period.

Authorities differ very widely as to the pathology of nasal lepra, and these differences of opinion, taken in conjunction with the recently asserted claims of the existence of primary leprous foci in the nose, tend to give the entire subject a unique importance.

Kaposi regards the pathological alterations in this locality as symptomatic rather than specific. Some regard the specific infiltration as confined to the anterior portion of the nose, and others find it everywhere.

It has usually been stated that while the cartilages are almost constantly attacked the bones are never directly affected, but Glück's numerous autopsies show that every bone in the osseous nasal framework may suffer directly. The same observer also refutes the prevalent view that the nose is not affected in anæsthetic leprosy. During the first outbreak of tubercular leprosy anterior rhinoscopy reveals a shining and congested mucous membrane. As there appears to be a great discrepancy of opinion as to this stage of leprosy, it may be well to follow Babes, who states that the initial manifestations consist of a diffuse and hardly perceptible leprous infiltration principally affecting the mucosa of the septum and lower turbinate body; this is accompanied by redness, induration, and increased secretion, and the latter may rapidly dry and contain abundant bacilli.

As for the subsequent stages of complete infiltration with partial resolution, destructive terminal alterations and collateral attempts at repair, hardly any two authorities draw the same picture. We may feel assured that the early infiltration may vary greatly. The deposit may be miliary or pea-sized, or may even exceptionally consist of a

single leprous tumor large enough to block the nostril and push the septum over into the opposite nasal chamber. This single large leproma is, of course, analogous to the tuberculous tumor described by rhinologists.

From analogy there can be little doubt that in an organ like the nose there must be two sets of manifestations, one specific and the other symptomatic. With regard to the leprous nodules, if they are small and scattered, it doubtless follows that a certain amount of resolution takes place. While the course of leprosy in the nose is acute, authorities appear to agree that leprosy here, as elsewhere, may occur in successive outbreaks, and that the earlier infiltration may be absorbed or may at any rate stop short of ulcerative or retrograde changes.

During this benign cycle the nasal mucosa can hardly avoid exhibiting evidences of symptomatic rhinitis. The localized leprous deposit must certainly be surrounded by areas of simple infiltration with thickening and increased secretion—in a word, hyperplastic rhinitis hardly differing from the same condition as it occurs under very different circumstances; and this hyperplastic stage must inevitably be followed by induration and sclerotic changes. All this is very obvious from the repeated statements of some authors, that nasal leprosy may occasionally terminate in a general sclerosis of the mucosa, without entering into any ulcerative or destructive lesions. Other authors speak of simple atrophy of the turbinates and amplification of the nasal chambers. In a word, in these benign and self-limited cases we have a picture not unlike ordinary hyperplastic and atrophic rhinitis. It is probable that this condition is exceptional, for a number of authorities do not describe it. The course of nasal leprosy being acute and quasimalignant as a rule, it is evident that the leprous infiltration tends to be extensive and that the specific manifestations usually predominate over the symptomatic. We may assume that the leprous nodules are prone to excoriation and later to ulceration, and that there is a discharge which is largely derived from these excoriated or ulcerated surfaces, and which may tend to form bloody, adherent crusts, which may occlude the nostrils and be detached with difficulty, or may occasionally flow from the nose. One of the results of this stage or degree of leprous rhinitis which is generally spoken of is the destruction of the columnar epithelia of thelia of the nasal mucosa; and after this stage of the disease, no matter to what further length it proceeds, the lining membrane undergoes a so-called "cutisation" which is almost universally mentioned in describing the nose in cases of inveterate leprosy—the membrane taking on the appearances of the skin.

This "cutisation" may not differ essentially from the sclerosis which has been mentioned as accompanying a relatively benign termination of the disease in so far that both processes involve a transformation of the columnar epithelial elements into the squamous form; but the former seems to result purely from specific changes and to accompany every case of inveterate leprosy, whereas the other process does not differ materially from that observed to follow simple hyperplastic rhinitis followed by sclerotic changes, and is evidently of exceptional occurrence.

Given that sooner or later in the typical case the nasal mucosa is largely occupied by a diffuse granulomatous infiltration chiefly specific in nature, the terminal lesions of the disease depend wholly upon the predominance respectively of the destructive or conservative process. If the granulation tissue tends to increase with only superficial ulceration, and with more or less cicatricial and sclerotic change, the nasal chambers are gradually occluded by the neoplastic tissue so that the so-called concentric narrowing of the nasal fossæ results. Here the mucosa of the septum, floor, and turbinates is equally enlarged and the nasal passage is largely obliterated. The phenomena of concentric narrowing and cutisation are mentioned by authors in large numbers of clinical histories of old leprosy. Another even more characteristic phenomenon has not yet been referred to, viz., absorption of more or less of the septal cartilage, which is extremely common. While this may be due also to other causes, it undoubtedly is often due to pressure upon both sides by the fungating granulomatous mass which has infiltrated the mucosa. Atresia of the nostril may be brought about in a manner similar to occlusion of the nasal fossæ, and it appears that all the foregoing changes of concentric narrowing, occlusion of the nostril, absorption of the septal cartilage, cutisation, etc., may occur without previous extensive ulceration, which latter phenomenon is somewhat less typical.

While a moderate degree of ulceration is sufficient to perforate the septum in many cases when the disease is by no means far advanced, these shallow ulcers which often heal over would not materially alter the picture which has already been described. More extensive forms of ulceration, however, occur at times, the ulcers being larger and deeper, and under these circumstances the turbinated bones may be destroyed outright, and extensive destruction of any of the hard and soft parts may result; and when these large and deep ulcers cicatrize, we may have deformity of the nostrils or adhesions between the outer and inner walls of the nasal fossæ.

All these types of advanced lesions of the inner aspect of the nose have their counterpart in infiltrating and destructive lesions of the

outer nose; Glück has described and illustrated several types of deformity due to both external and internal lesions: the nose may be twisted to one side, it may be flattened like the negro nose, or it may overhang the upper lip.

The Internal Organs.

Lymph Ganglia.—The cervical, axillary, and inguinal glands are most commonly affected, with occasionally the visceral (mediastinal and retroperitoneal). The ganglia are enlarged and show cheesy or hyaline foci, and in old cases chalky deposits with sclerotic changes. The adenoid tissue wholly disappears.

Blood-vessels.—Peri- and endoarteritis and phlebitis occur, with resulting narrowing of the lumen and at times thrombosis. These changes are usually due to the proximity of leprous foci, but the fact that vessels become leprous when no such foci are near appears to show that metastases must occur through the circulation. Glück has called attention to the lesions of the large subcutaneous veins, which he declares are by no means rare. Leprous phlebitis is manifest in the form of a nodose tract, distinctly limited, sometimes without any connection with neighboring tubercles, occupying any portion of the vein which may be healthy above or below; sometimes a series of nodose lesions may be observed upon the same vein. Upon histological examination after excision, there are found thickening of the adventitia, with infiltration of small cells in the muscular coat, and considerable thickening of the endo-vein with new formation of the capillaries. In all the tumors, and even in the endothelium, bacilli are abundantly present with their characteristic disposition. Glück contends that the bacilli may penetrate the walls of the vessels from without.

Spleen.—Bacilli are always present here, even when no pathological changes are evident. When the spleen is structurally altered the lesions are analogous to those observed in the lymph ganglia. Joseph found large quantities of bacilli in the spleen in cases in which the most minute research could not detect them in the liver, kidneys, or other viscera. He suggests a relation between the abundant presence of the bacilli in this organ and its function in the formation of blood.

Bone Marrow.—The fatty tissue disappears and the marrow becomes firm and takes on the appearance of hæmatopoiesis. Hæmatoblasts, new-formed capillaries, nucleated red blood corpuscles, proliferation of large round cells, and myeloplaxes occur.

Lungs.—The lungs of lepers are either normal or exhibit the

lesions of tuberculosis. Leprous foci may, however, occasionally occur. They consist of thickening of the interstitial tissue with compression and obliteration of the alveoli.

Intestine.—The intestinal ulcers often found in leprosy are tuberculous, but occasionally true leprous lesions have been met with (eroded nodular areas). Bacilli have been found in ordinary intestinal mucus.

Liver.—In the liver we get increase in the volume of the interstitial tissue, with new formation of the radicles of the bile ducts. Amyloid degeneration has occasionally been recorded.

Kidneys.—Bacilli have been found in the tumefied endothelium of the vessels of the kidney, especially in the glomeruli and also in the suprarenal bodies.

Babes has found the bacillus in the brain, pancreas, hypophysis cerebri, thyroid, prostate, and in tissues which were apparently altogether healthy.

Female Breast.—In tubercular leprosy the bacillus has been found in the milk. In cutaneous leprosy the infiltration extends inwards along the ducts, and often penetrates the membrana propria and epithelial layer. Bacilli have been found free in the acini and ducts.

Testicle.—This is a locality of early and constant implication. The gland is often affected when apparently normal, and its function may be compromised or entirely destroyed during the first or second year of the disease. In a typical case the changes are chiefly interstitial—proliferation of the intercanalicular septa and membrana propria, with resulting compression of the canaliculi. Necrotic foci may appear in the infiltration. The cord remains intact for a long time.

Ovaries.—Bacilli have been found, but not under such circumstances that sexual infection could be assumed. There are but few bacilli to be found and few anatomical changes.

Anæsthetic Leprosy.

The appearance of the nerves in leprosy varies extremely according to the kind of leprosy, stage of the disease, and size of the nerve invaded. Even in ordinary leprosy of the skin, when the terminal nerves are involved as part of the general infiltration, bacilli may be found higher up in the course of the nervo trunks, while in certain infiltrated patches of skin the bacilli and neoplastic tissue may be confined to the skin and their immediate periphery.

The diseased nerves appear greatly thickened, both the peri- and endoneurium having undergone proliferation. This infiltration is characterized by the presence of large, round, or elongated cells, containing the bacilli more or less abundantly. Between the atrophying nerve fibres or replacing them are found large fusiform spaces, which are replete with colonies of bacilli. In the smaller peripheral nerves, then, we find proliferation of the epi- and endoneurium, with retrograde changes in the nerve fibres.

In the large trunks, such as the median, we find proliferative changes in the epineurium, in the connective-tissue septa, between the bundles of nerve fibres, and, finally, in the special investment of individual fibrillæ. The cellular elements arise chiefly from the endothelia of the vessels and fixed connective-tissue cells. The bacilli in the nerves lie between rather than within the cells, and may be found within Schwann's sheath. The nerve elements proper show numerous retrograde changes.

Spinal and Sympathetic Ganglia.—Bacilli occur within the large cells of the spinal ganglia, lying within vacuoles. They are less numerous in the sympathetic ganglia. Nearly all the bacilli lie within the cells, but in certain cases the capsule and interstitial connective tissue are affected, and the ganglia in these cases are thickened. A remarkable fact is that the nerve fibres which are continuous with the ganglia as well as the blood-vessels appear to be free from bacilli.

Spinal Cord.—Single bacilli may occur in perfectly normal ganglionic cells; eventually they lead to disappearance of the chromatic substance and pigment, and of the nucleus itself. Vacuolization is general throughout the cell.

The presence of bacilli in the cord is not known to cause any special symptoms. Babes found bacilli in the cord in nine cases, three times in the anterior horns; in pure lepra nervosa the bacilli have never been found in the cord. On the other hand, the spinal ganglia are almost invariably implicated in nerve lepra. Owing to the extensive implication of the peripheral nerves, it is difficult to determine the influence, if any, of ganglionic leprosy. The presence of bacilli in the spinal cord has naturally an important bearing in connection with the origin of syringomyelia and also in the interpretation of the pathogeny of the habitual symmetry of anæsthesia and the amyotrophic disorders of leprosy.

Jeanselme, in two out of five autopsies, found a pronounced degeneration of the posterior column, and in one of the cases similar changes in one of the lateral columns. The topographic disposition explains, he thinks, certain tabetiform troubles which have been

observed in leprosy. The whole question of the relations of the leprous process to disorders of the central nervous system is unsettled and involved in much obscurity. There is a marked divergence of opinion between histologists as to the interpretation of the nervous manifestations. Dehio, Looft, and others claim that the nerves are always invaded by their peripheral extremities, and that their infection as well as their degeneration always follows a centripetal course, with successive implication of the motor and sensory collateral branches. Darier has suggested the probability that the pathogenic process is not the same in all cases—that sometimes the centres, sometimes the peripheral nerves may be primarily invaded by the bacillary proliferation.

DIAGNOSIS.

A retrospective diagnosis of the diseases formerly classed as leprosy would show that a vast number of ordinary dermatoses were included in this category. In the light of our present knowledge it would appear that the leprosy of Mosaic times embraced vitiligo, psoriasis, scabies, certain forms of eczema, and perhaps other diseases.

In the Middle Ages the greatest chaos and confusion prevailed in the classification of diseases of the skin. On account of the vagueness of the terms then used in describing skin diseases, and the difference in the signification attached to them in modern dermatological nomenclature, it would be impossible to indicate accurately what the leprosy of that period included. It is very probable that the population of the numerous leproseries which were established in various parts of Europe during mediæval times was largely swollen by the inclusion of a vast number of persons suffering from diseases of the skin of an entirely different character—many of them not in the remotest degree contagious. It is very certain that many types of disease which have recently been recognized as distinct morbid entities were confounded with leprosy, such, for example, as syringomyelia, morphœa, scleroderma, mycosis fungoides, and Raynaud's disease. It is very probable that psoriasis, pemphigus, pellagra, scrofula, lupus, syphilis, and other diseases which presented some objective resemblance to leprosy were classed with the latter disease.

One of the most mysterious problems in the history of medicine, which has not yet received a definite solution, was the sudden apparition of syphilis in Europe towards the close of the fifteenth century, and the displacement of leprosy by the new disease. There can be no doubt that the multitudinous cutaneous manifestations of syphilis and their similitude to leprosy, a similitude rendered more striking

by the epidemic violence with which syphilis then raged, furnished an admirable field for error, and that syphilitics contributed a large contingent to the resident population of the leper houses. Guy Patin tells us that at the beginning of the sixteenth century "the leproseries were filled with syphilitics." The extent to which leprosy prevailed in Europe during the Middle Ages and the actual number of lepers imprisoned in the nineteen thousand leper houses were doubtless magnified by the indiscriminate segregation of all persons whose symptoms bore any resemblance to those of leprosy.

The clinical picture of leprosy which is drawn by text-book writers of the present day is that of a disease which is as readily recognizable by its typical features as it is repulsive by its hideous deformity. This common conception is derived from examples or representations of the disease in its fully developed or final stage. With its initial manifestations and the varied phenomena exhibited in the earlier stage of its evolution, few medical men except those resident in leprous countries are familiar. While it is undoubtedly true that the clinical features of a case of tubercular leprosy, typical in its development and advanced in its evolution, are so striking and characteristic as to be absolutely pathognomonic, it is equally true that in its earlier stages, and even in fully developed cases with atypical manifestations, there is no disease in the entire domain of pathology more difficult of recognition.

This observation applies with still more force to anæsthetic leprosy. Reference has already been made to many forms of disease which have but recently been recognized as distinct types, but which imitate the phenomena of nerve leprosy so accurately that the differentiation cannot always be established from the objective characters or the sensory disorders. This similitude is so marked that certain leprologists maintain that these diseases are survivals of leprosy and represent abortive or degraded forms of the disease. Even so distinguished an authority as Erasmus Wilson declared in 1862 that the various forms of morphœa and alopecia areata are manifestations of leprosy. Kaposi also describes morphœa as a form of macular leprosy. Eastlander regards mal perforant as the last vestige of leprosy in France.

The difficulties which attend the diagnosis of leprosy depend upon its prolonged period of incubation, the absence of any initial lesion that might connect it with a known exposure, the indeterminate character of its prodromal symptoms, and finally the multiplicity and banality of its manifestations. The fact that leprosy is essentially a proteiform malady is not sufficiently appreciated. While syphilis may surpass it in the number and variety of its eruptive elements,

the cutaneous manifestations of leprosy most accurately imitate many of the ordinary dermatoses. This imitation is carried into the realm of neuropathology, nerve leprosy simulating most deceptively the manifold forms of neuritis of toxic, traumatic, and constitutional origin.

The early manifestations of leprosy, unlike those of syphilis, are in no sense peculiar to the leprous process. There is nothing regular in their mode of evolution, nothing constant in their appearance, nothing distinctive in their morphological characters. They are so variable, uncharacteristic, and absolutely indefinite that they would never be ascribed to leprosy in any country where the disease was not endemic, or where there were not decided reasons for suspecting its presence. This emphasizes what may be considered a point of cardinal importance in the diagnosis of leprosy. Since leprosy is exclusively human in its origin, the history of known contact with a leper or residence in a leprous country is of the greatest diagnostic worth.

Obviously enough the difficulties of diagnosis are increased in non-leprous countries where an opinion must be based upon the objective characters alone and where the absence of a history of known exposure withholds the necessary confirmation of its correctness. This fact has been forcibly impressed upon me in the case of the patient pictured in Fig. 11, in which there was no clear history of exposure. The attending physician, Dr. MacDougall, in sending the additional notes of the case, remarks: "In connection with the diagnosis of these cases I am inclined to believe that some censure is due leprologists for their positive statements that the manifestations of the disease, when at all advanced, are so characteristic that there can be no mistake."

Incidentally it may be said that a picture of these patients was submitted to a number of specialists in skin diseases, none of whom would admit the diagnosis of leprosy because there was no clear history of exposure, and yet if they had lived in a leprous country there could have been little doubt as to the nature of the trouble.

Erasmus Wilson cites a case of a medical man in the Indian army, himself a leper, but who with other medical men in India regarded his case as syphilis. A case of Hutchinson was treated for several years for rheumatic gout. The man had pricking pains in the fingers, as well as numbness and insensibility, and was unable to write. Another of Hutchinson's patients was treated for two years by nerve specialists for paralysis affecting the ulnar nerve.

Thin cites numerous examples of cases erroneously diagnosed by observers experienced in dermatology; for example, that of

a patient with a well-developed nerve leprosy, who was sent home from India as a case of lupus erythematosus; two other cases in which typical anæsthetic patches with pigmentary changes were wrongly diagnosticated.

A case of Abraham was for a long time confounded with carcinoma.

Instances might be multiplied of cases of leprosy which exhibited sensory and even advanced trophic changes, the nature of which was unrecognized. A patient of mine was for several months under the care of one of the most distinguished leprologists of Europe without his suspecting the nature of the disease, until his perceptions were quickened by accidentally learning of the patient's former residence in a leprous country.

Mistakes in diagnosis are by no means confined to physicians in non-leprous countries. Even so competent a clinician as Beaven Rake, whose long residence in Trinidad made him familiar with every possible feature of the disease, reports a case in which leprosy was by him mistaken for syphilis, an error which was confirmed by the temporary disappearance of the tubercles under mercury, but which was corrected by the subsequent redevelopment of the tubercles with other unmistakable signs of leprosy.

In attending numerous examinations of persons arrested as lepers in the Hawaiian Islands and sent to Honolulu to be examined by the examining board, I was impressed by the large proportion of cases placed in the category of "suspects," embracing those presenting suspicious symptoms, but in whom evidences of the disease were not sufficiently clear and unequivocal to warrant their consignment to the leper settlement of Molokai. Although the examining board was made up of physicians presumably familiar with every phase of the disease and who were especially selected for their diagnostic ability, there was in many cases much confusion as to the nature of the eruption, especially when in the early erythematous stage. There is no doubt that it requires a nice judgment and a thorough acquaintance with the incipient evidences of the disease to discriminate between leprous macules and an erythematous eruption due to other causes. Notwithstanding the precautions taken to avoid an erroneous diagnosis it frequently happened that persons were wrongly declared lepers, and in order to rectify possibly unjust sentences a medical commission was appointed by the board of health to visit the leper settlement at stated intervals and reëxamine persons enrolled on the list of lepers who claimed that they did not have the disease.

Tubercular Form.

The *prodromal symptoms* which precede the eruptive stage of the tubercular form possess but little diagnostic value. Similar symptoms may be present in the secondary incubation of syphilis or other infectious diseases. The initial pyrexial symptoms present nothing distinctive. The attacks of fever succeeded by profuse perspiration are frequently mistaken for ague. If the fever be followed by an erythematous eruption which tends to become fixed, suspicion should be excited, especially in a country where leprosy is prevalent. The significance of other prodromal symptoms, as epistaxis, cephalalgia, general malaise, etc., is seldom recognized until objective signs of the disease are manifest, and then they are, of course, valuable as a retrospective aid in diagnosis. The sensory disorders which form so valuable an element in the diagnosis of anæsthetic leprosy frequently fail in the tubercular form, and their presence or absence may be disregarded. Among the diseases with which the tubercular form of leprosy may be confounded are certain dermatoses of the erythematous type, various pigmentary affections of the skin, acne indurata and rosacea, sycosis, erythema nodosum, molluscum, psoriasis, syphilis, lupus, mycosis fungoides, etc.

Erythema.—The macular lesions which ordinarily constitute the first cutaneous manifestations of leprosy present nothing absolutely distinctive either in their objective characters or course. Leprous roseola at its first appearance may be mistaken for a variety of simple erythematous eruptions. Lailler, one of the most experienced French dermatologists, says that he has mistaken a case of leprous erythema for the erythema produced by the ingestion of strawberries. The error was cleared up only by the persistence of the eruption.

The exanthem sometimes resembles that of the eruptive fevers. I have recently seen a case in which the initial rash had been diagnosticated as measles, from which it was differentiated by its persistence. During three years it faded and reappeared a number of times in the form of erythemato-papular lesions before the characteristic tuberculation took place.

Chronic dermatitis is distinguished from leprosy by the more general and uniform thickening of the skin and the absence of tubercles.

Parasitic Affections.—Ringworm and chromophytosis may be mistaken for leprous spots. In tropical countries, as in Hawaii, parasitic skin affections often exhibit a luxuriant development unknown in cold or in temperate climates. Not infrequently parasitic diseases coexist with leprosy and may mask the manifestations of the latter

disease. An examination of the scales and scrapings will always identify the parasites if present.

Acne Indurata and Rosacea.—Hebra instances cases in which leprosy has been mistaken for these forms of skin affection. Impey, who has had large opportunities of studying the clinical aspects of leprosy in South Africa, says: "I know of no other disease which may be so readily mistaken for leprosy as rosacea." The eruption of gutta rosea is to be distinguished by its localization on the chin, cheeks, and nose and the exemption of the eyebrows. In rosacea there is a more uniform thickening of the skin over a large area—the color of the eruption is more uniform than in leprous erythema, the hairs are not lost, and the scales are more abundant. In leprous erythema there are no enlarged vessels to be seen, the color of the patch is of a darker hue in the centre and gradually fades into the surrounding skin, the hairs are soon lost from the leprous patch.

Sycosis is another affection of the face for which leprosy may be mistaken when the tubercles are limited to the hairy parts of the face.

Lichen Planus.—When the neoplasms are small, flattened, and closely aggregated tubercular leprosy has been confounded with lichen planus.

Molluscum Fibrosum.—One of my colleagues in New York exhibited a case in which leprous nodules had been mistaken for the tumors of molluscum.

Keloid has been confounded with leprosy. It is to be distinguished by its hard, fibrous base, its resemblance to a cicatrix, and other objective characters, besides being commonly unilateral.

Erythema Nodosum.—When the nodules are situated along the external malleolus and the front of the leg, they bear a most deceptive resemblance to the nodules of erythema nodosum. Leloir mentions cases in which the size, shape, and disposition of the lepromata were strikingly suggestive of this disease. The more or less rapid involutionary changes of the nodules in the latter disease would, of course, soon clear up the diagnosis.

Psoriasis was at one time considered a form of leprosy. It may be admitted that there was perhaps a superficial basis for this erroneous view in the objective resemblance between psoriasis gyrata and the circinate lesions of leprosy. The tendency of psoriatic patches to enlarge peripherally and form by their confluence circular and gyrate forms gives them a configuration not unlike the circinate and concentric bands, especially seen in the anæsthetic form of the disease. Circinate psoriasis is, however, readily differentiated by its tendency to epidermic proliferation in white or grayish scales, distinctly imbricated, which, when removed, show a well-defined infiltration elevated

at the border, depressed in the centre, with a hyperæmic, readily bleeding surface. From the exceeding commonness of psoriasis in all countries and in all ages, it is evident that sufferers from this disease must have figured largely in the population of leper houses.

Syphilis.—The old view that "syphilis was the daughter of leprosy," which was based upon the fact that an epidemic of syphilis made its appearance at a period corresponding to the decline of leprosy in Europe, has been long exploded. We now recognize that the relation was coincidental rather than causal, and that each is a disease *sui generis*. That they are totally unrelated to each other is proven by the independent development and coexistence of the two morbid states in the same patient, each running its own course. That "leprosy is more common in the children of syphilitic parents," as has been maintained by many authorities, may be admitted on the ground that a native debility in the offspring of syphilitics, like any other ancestral cause of weakening, may predispose to leprosy.

Syphilis presents many clinical analogies with leprosy, both in the polymorphous character of its manifestations and their mode of evolution. In both, the general accidents develop after a prolonged period of incubation. Syphilitic roseola has its analogue in leprous erythema; syphilitic pigmentation in the pigment spots of leprosy; syphilitic alopecia in the alopecia of leprosy. The papules and tubercles of syphilis have their counterpart in the dermic and hypodermic nodules of leprosy. In both, the neoplasms follow a similar course of involution; they may undergo resorption, or they may soften and suppurate and disappear by a process of ulceration, sometimes involving extensive surfaces and leaving characteristic cicatrices. Their points of dissimilarity are, however, too numerous and obvious to merit mention.

The erythematous syphilide may be distinguished from leprous erythema by the smaller size and fainter coloration of the lesions, their absence from the face and limitation to parts habitually covered by the clothing, and their more rapid disappearance. The erythematous patches of leprosy are larger, more diffuse, and more permanent. The pigmentations of leprosy are readily distinguished from the posthumous pigmentations of syphilitic infiltrations. The lenticular tubercles of leprosy, when they are disseminate, small, slightly elevated, with moderate desquamation, may resemble absolutely a papular syphiloderm. It is, however, the tubercular form of syphilis which bears the most deceptive resemblance to leprosy.

The clinical features of the case of tubercular leprosy represented in Fig. 3, are seen to simulate almost accurately a tubercular syphilide. The syphilitic nodules are more circular in outline, more reddish-

brown or coppery in color, more apt to be grouped in circular and crescentic forms, and more rapid in involution. The ulcerations of syphilis are more rounded, less circumscribed in extent, the crusts are thicker, harder, and of a brownish, blackish, or greenish tint. Leprous ulcerations progress more slowly than those of syphilis, and they do not present a serpiginous mode of extension. The extensive superficial infiltrations of leprosy are not seen in syphilis. Leprous neoplasms are larger in volume, more protuberant, and crowded upon an infiltrated base, with œdema of the skin and ganglionic enlargements. Their seats of predilection are the facial mask, the lobes of the ears, backs of the hands, and forearms, more rarely disseminated, while the nodules of syphilis are indiscriminate in their location and may come where leprous tubercles rarely or never appear. The leontiasis of leprosy is much more pronounced than that of syphilis. The enormous nodular masses, the deep orbital and supraorbital furrows, the pillowy-like protuberances of the cheeks, with loss of the eyebrows, are never observed in syphilis. Still, in many cases of less exaggerated development the facies of leprosy may simulate most closely that of syphilis.

Lupus Vulgaris.—This form of cutaneous tuberculosis shares with leprosy the pathological peculiarities of cell infiltration of the connective tissues of the skin, followed by disintegration of the morbid products and ulceration. Leprosy may be mistaken for lupus vulgaris, especially when the leprous lesions consist of small brownish-red tubercles grouped upon a reddened infiltrated base and localized upon the cheeks and face; the frequent involvement of the lobe of the ear in lupus heightens the similitude. Lupus is distinguished by its occurrence in the form of isolated patches and its more limited localization; it is commonly unilateral and not accompanied by disorders of sensation. In all doubtful cases of tubercular leprosy the demonstrable presence of the bacilli in the tissues or liquid exudates establishes the diagnosis.

Lupus erythematosus may also be mistaken for leprosy. I have been consulted by a leprous patient, the right side of whose forehead and cheek was occupied by slightly raised erythematous patches of a sombre red color simulating perfectly lupus erythematosus. The latter disease may be usually distinguished by the configuration of the patches which often assume a butterfly shape, by the central depression of the plaque and the greasy adherent scales which often dip down into the follicles, and by its limitation, as a rule, to the face.

Mycosis Fungoides.—On account of the numerous and marked analogies between this disease and leprosy in their evolutionary mode and the objective character of their phenomena, mycosis fungoides

has been not inaptly designated by Bazin as *indigenous* leprosy. Both diseases are characterized by an eruption of erythematous spots or patches, which may appear and recede a number of times before becoming permanent. These patches are the seat of the neoplastic formations peculiar to each disease.

In the premycosic stage the efflorescences are at first transitory, but they grow more and more persistent until they become permanently established under the form of reddish, slightly scaly, or lichenoid plaques. After the lapse of time more or less variable these plaques become the seat of red or violaceous tumors, isolated or grouped, which may remain stationary, undergo involution by a process of resorption and become effaced without leaving a trace, or break down and become fungous and ulcerating. A further similitude to leprosy may be noted in the sensory disorders which are frequently manifest. The surface sensibility is sometimes markedly diminished, the hairs may become atrophied and disappear; the lymphatic glands become tumefied and swollen. Both diseases almost invariably progress to a fatal termination. The resemblance to leprosy is most marked when the lesions of mycosis are localized upon the face. As differential points may be mentioned the constant and intolerable pruritus of mycosis, which is almost invariably present. In the tumor stage the soft, dough-like masses with their fungating, tomato-like appearance present a picture unlike that of leprosy. The presence or absence of the bacillus lepræ will set aside all doubt as to the diagnosis.

Multiple sarcomata have been mistaken for leprosy. The development of these tumors is rarely preceded by the appearance of erythematous patches, and their localization is different.

Alopecia.—The alopecia of leprosy is characterized by the atrophy and disappearance of the eyebrows and lashes, the vibrissæ, and the hairs from other portions of the body the seat of leprous lesions, while the hair of the scalp is not much affected.

Leprosy of the Mucuous Membranes.

A new and unique interest has been given to the diagnosis of leprosy of the nasal mucous membranes owing to the now generally recognized precocity of their appearance. Leprosy in the early stage often simulates catarrhal inflammation of the nose. Since leprous rhinitis is dependent upon the presence and local action of the bacilli upon the Schneiderian membrane, the diagnosis may be established by bacteriological examination of the nasal secretions which, especially in the tubercular form, contain them in large numbers. Epi-

staxis is a more constant accompaniment of the leprous process than of an ordinary rhinitis.

The diseases affecting the mucous membranes of the mouth, nose, and throat which may be confounded with leprosy in a more advanced stage are few. They all belong to infectious diseases of the granuloma type, and while offering a great similarity of aspect, they are distinguished by certain special characters.

Syphilis.—Syphilitic infiltrations of the nasal mucous membranes bear a deceptive resemblance to those of leprosy. They affect the framework of the nose and are often followed by extensive destruction of the tissues and resulting deformities. Syphilis is, however, more liable to attack the osseous framework of the nose, producing a sinking in or falling of the bridge of the nose. The deformation of the nose in leprosy is commonly due to a destruction of the cartilaginous septum which leads to flattening and broadening of the alæ, which fall and become spread out from the loss of natural support. Syphilis may also occasion destruction of the septum.

A rhinoscopic examination of the leprous nose in the tubercular form will reveal the presence of small tubercles disseminated upon the septum, sometimes over the turbinated bones, with ulceration. The presence of anæsthesia also serves to indicate the leprous nature of the changes.

The syphilitic affections of the tongue, the buccopharyngeal cavity, and the larynx often bear a deceptive resemblance to those of leprosy. Leloir has called attention to the occurrence of forms of leprous glossitis which recall similarly appearing sclerogummatous infiltrations of syphilis.

Leprosy of the mouth and throat exhibits in the localization and size of the tubercles, which are usually small and disseminate, certain objective characters not seen in syphilis. The ulcerations of syphilis are more profound and extensively destructive and the ulcerative process is more acute. The complete abolition of ordinary sensibility and the conservation of the sense of taste in its integrity are characteristic of the leprous process.

Lupus produces alterations of the nose quite different from those occurring in leprosy. Lupus exhibits a marked tendency to implication of the soft tissues with more or less infiltration and sclerosis. The alæ of the nose are nibbled by ulcerations, and the nose itself is shortened and thinned, contrasting with the nose *en lorgnette* of leprosy. Even when lupus destroys the septum, the sclerosed tissues support the structure and prevent the falling and flattening observed in leprosy. Besides, the lupous process is more chronic and persistent in its morbid pertinacity, rarely relaxing its work until the cu-

taneous covering of the cartilaginous segment of the nose is entirely destroyed.

Glanders, which is comparatively rare in the human subject, may also simulate leprosy of the mucous membranes in the production of small barley- to pea-sized tubercles, isolated or confluent and disseminated over the cartilaginous septum and the turbinated bones. These may break down and ulcerate with the production of a purulent or mucopurulent secretion. Similar processes may also affect the mucous membranes of the eye, the mouth, and the throat. Glanders may always be identified by the presence of the bacillus mallei, which is readily inoculable to animals.

In the differentiation of leprosy from the above group of diseases, the history, the concomitant evidences of skin trouble peculiar to each disease, and the presence or absence of anæsthesia, which is pathognomonic of leprosy, are usually quite sufficient, independent of a bacteriological examination of the secretions.

In addition the obstruction of the nostrils, the harsh, raucous, or croaking voice of leprosy, the difficulties of deglutition and respiration, and the peculiar, foul leprous odor exhaled by the breath are all characteristic features.

The Anæsthetic Form.

The *prodromal symptoms* are much more variable, but scarcely more characteristic than those of the tubercular form. The sensory disorders, hyperæsthesia, formication, pruritus, and sensations of burning and tingling, have little diagnostic value, as they may be present in irritative neuritis from other causes. The pain and motor weakness often present are commonly ascribed to rheumatism or neuralgia. At a more advanced stage the presence of anæsthesia constitutes an almost invaluable diagnostic element as the identification of the bacillus in the tissues is rarely practicable in nerve leprosy.

The erythematous spots of the anæsthetic form are characterized by their permanence, their tendency to clear in the centre while spreading peripherally, their achromatic changes, and at a more advanced period by their anæsthetic centres.

Chromophytosis.—The pigmented spots may be yellowish or fawn colored, giving quite a deceptive resemblance to chromophytosis. The patches of the latter are furfuraceous and may readily be removed.

Ephelides.—In one of Hutchinson's cases the first symptoms were large freckles on the forehead, followed by a general exanthem and dulled sensation.

Chloasma has been confounded with the pigmented patches of

leprosy. Quite recently a case came under my observation in which this mistake had been made.

Pellagra, acrodynia, and chronic ergotism may be mistaken for the pigmentations of leprosy. In pellagra the brownish-red, erythematous patches, the appearance of bullæ, the atrophic changes, and paralysis of the third nerve make up a clinical picture which bears a most deceptive resemblance to certain phases of leprosy.

Scleroderma and sclerodactylie, that form of the affection in which the atrophic troubles are limited to the extremities, may be confounded with leprosy. Scleroderma is characterized by induration followed by atrophy of circumscribed portions of the skin which are more or less diffused and symmetrical. The patches are white, often of a yellow or old-ivory color, the secretions of the sebaceous and sudatory glands are diminished, as in leprosy, and the sensibility is first increased and then diminished. Subcutaneous tubercles have been observed in a few cases. The objective differences between leprosy and this form of the disease are so marked as scarcely to permit of the possibility of a mistake in diagnosis.

The trophic changes met with in *sclerodactylie*, characterized by distortion of the phalanges, alterations of the nails, and the ulcerations which are not uncommon, present a much greater similitude with leprosy. They are to be differentiated by the absence of the concomitant signs of leprosy.

Morphœa.—Erasmus Wilson describes morphœa alba, lardacea, and nigra as forms of local leprosy. Kaposi has followed his example in identifying these varieties of morphœa with macular leprosy. While morphœa may present a certain resemblance in color, form, and distribution with the sclerotic patches of leprosy, yet it is readily differentiated. The plaques of morphœa are lardaceous or wax-white in appearance, of a hard, unyielding consistence, and surrounded with a violet or lilac ring which is most characteristic, and in addition the sensory disorders of leprosy are absent. Some three years ago a case of morphœa came under my observation which had been diagnosticated by a number of physicians as indigenous leprosy.

Vitiligo.—The achromatic spots of nerve leprosy may be mistaken for vitiligo. The patches of vitiligo are of an irregular shape, of a dead-white color, perfectly smooth surface, and with margins convex and clearly defined against the surrounding pigmented border, which has a tendency to spread peripherally. With the exception of the dyschromia the skin is unaltered in structure and the sensibility is unchanged; the hairs of the affected surface are often white, but do not fall. In leprous leucoderma, which is most often seen in dark races, the spots are grayish-white and not so sharply defined in contour.

The skin is altered in structure with atrophy of its glandular apparatus, atrophic, depressed, sometimes corrugated, and commonly completely anæsthetic. The hairs are not invariably white and often fall from the patch. The evolutionary mode is entirely different. While the leprous achromatic spots may appear as such from the first, they are ordinarily formed by a pigmented patch becoming white in the centre with coincident loss of sensation.

Pemphigus Vulgaris.—The pemphigus blebs which characterize nerve leprosy may be mistaken for pemphigus vulgaris. The bullæ of leprosy may be distinguished by their sparser numbers, their more superficial characters, their localization, their tendency to come out in successive crops, their characteristic cicatrices when they become ulcerated, and by the sensory disorders which ordinarily accompany or succeed them.

In many cases leprosy pursues an anomalous course. The macular, pemphigoid, and other trophic changes may be absent, and motor and sensory disturbances constitute the only manifestations. There are many diseases depending upon lesions of the peripheral nerves and cord the symptoms of which may be accurately simulated by leprosy. When these neuritic changes are accompanied by the presence or history of leprous exanthems, or phenomena of hyperæsthesia and anæsthesia, swelling of the nerves, disturbances of the sweat function, leprous coryza, etc., there is no difficulty in diagnosis; but when such concomitant evidences fail, and the paralytic and atrophic changes constitute the sole objective signs, remaining stationary and persisting for months or years, the diagnosis may become exceedingly difficult.

The phenomena of leprous neuritis constitute a distinctive feature of great diagnostic importance. The ulnar nerves are usually primarily involved, but not invariably, as affections of the nerves of the legs may be first manifest. In many cases patients complain of numbness and weakness in the muscles of the foot and extensors of the toes, which are due to beginning atrophy of the peronei and extensors. In the majority of cases the ulnars are the first to manifest evidences of inflammatory and degenerative changes accompanied by the atrophic changes in the hands and forearms already described.

The paralysis may in some cases appear first in the orbicularis palpebrarum and other muscles supplied by the cranial nerves, rendering it impossible to close the eyes, or the face may be drawn to one side.

Progressive muscular atrophy may be confounded with leprosy. There is the same wasting of the interossei, of the thenar and hypothenar muscles, with paralysis of the extensors resulting in the *main*

en griffe characteristic of leprosy, but the muscular atrophy is differentiated by the absence of anæsthetic patches and thickening of the nerves.

Paralysis agitans is another affection for which leprosy has been mistaken. Impey mentions a case he found in the leper ward of this form of paralysis. The patient was unable to walk or even leave her chair. Constant friction had caused extensive ulceration of one foot. Both feet were much deformed and the hands were contracted but there were no anæsthetic patches and the eyes were unaffected.

Multiple neuritis of toxic or malarial origin presents many analogies with the earlier stage of anæsthetic leprosy, but is distinguished by its more acute course and the absence of anæsthetic patches.

Arthritis Deformans.—The characteristic deformities of the hands and feet caused by chronic rheumatism have been confounded with those of leprosy. This mistake is all the more liable to occur as the muscular pains and other early phenomena of leprosy are often attributed to rheumatism. The swollen joints of arthritis do not occur in leprosy, and there is an absence of localized morbid deposits, the changes in leprosy being essentially atrophic.

Perforating Ulcer.—The plantar ulcer of leprosy bears a most deceptive resemblance, both in objective characters and course, to the *mal perforant*, which may be due to atheromatous changes or of purely nervous origin. In the latter affection the concomitant symptoms of leprosy are absent.

The lesions of the bones and joints with deformities and mutilations which commonly occur in the advanced stage of nerve leprosy can scarcely be confounded with the changes occasioned by other diseases. Yet Impey reports that he found in the Robben Island Asylum one patient who had lost his toes from the necrosis of frostbite; another had been sent there because he had lost his feet by gangrene. "The latter patient was kept in the leper asylum for many years without any suspicion having apparently been raised as to the true nature of the disease or deformity."

Syringomyelia.—This disease, which may no longer be considered a pathological rarity, presents the closest clinical analogies with nerve leprosy, and their differentiation may be difficult or impossible. There is such a striking similitude in their course and symptoms that the error of confounding them is almost inevitable in the absence of the prior manifestations and etiological history of leprosy. Leloir and Dejerine have reported cases in which the diagnosis was extremely difficult. It is only in the anæsthetic period of leprosy that confusion is likely to arise.

The more prominent and distinctive clinical features of syringo-

myelia may be thus summarized. There is an absence of surface discolorations or characteristic spots on the skin; a complete integrity of the muscles of the face; a conservation of the integrity of the pilous system; a disassociation of the different modes of sensation; the sensibility to pain, to heat, and cold is abolished, with integrity of the tactile sensations. In addition there is frequently a deviation of the vertebral column.

In leprosy, tactile sensibility is most frequently abolished; there are atrophy and paralysis of the superficial muscles of the face; double paralysis of the orbicular muscles; thickening of the nerve trunks, especially the ulnars, with nodular swellings; pigmented or achromatic patches which may be anæsthetic, dystrophia of the extremities; spontaneous loss of the phalanges, alterations or loss of the nails, and alopecia. The difficulty of diagnosis is complicated by the fact that it is not always possible to demonstrate the presence of the bacillus in nerve leprosy.

While the sensory disorders in leprosy and syringomyelia present numerous points of resemblance, their distinctive characters have been thus differentiated by Jeanselme:

"The anæsthesia of leprosy is always symmetric, at first ribbon-like, later segmentary, imperfectly disassociated and of an intensity gradually decreasing in going from the surface of the skin to the deeper portions and from the free extremity of the limbs to their root. The anæsthesia of syringomyelia is often asymmetric, segmentary from the first, in general perfectly disassociated and separated by a sharp limitation of the superficial and subjacent sensible regions.

Finally may be mentioned those *atypical* forms of the disease in which a deviation from the normal plan of evolution introduces an element of confusion in diagnosis. While as a rule the lesions of leprosy are more or less symmetrical, cases are met with in which the manifestations are strictly unilateral. I have had under observation a case in which twelve years after infection the only symptoms were dystrophia and anæsthesia of the right hand, forearm, and ankle; another of ten years' duration in which the manifestations were limited to three or four erythematous patches with anæsthetic centres on the left side; still another of mixed leprosy in which the sole signs of the disease were a single tubercle on the right cheek and anæsthetic changes in the right hand.

Quite recently I have seen a case in which the erythematous patches were symmetrical, but the trophic changes were absolutely unilateral and limited to complete disorganization of the right ulnar nerve, the parts supplied by which were insensitive to pressure, atrophied, and wasted, and there was a characteristic claw-like defor-

mation of the right hand. The left ulnar nerve was apparently normal, and the muscles of the left hand and arm were unaffected. There was no appreciable involvement of the nerves or the muscles of the face. Even the eyelashes were conserved in complete integrity.

While the cases seen in non-leprous countries are perhaps more apt to exhibit atypical manifestations, yet even in countries where leprosy is endemic the same peculiarity is manifest. In the leper settlement of Molokai, according to Mr. Dutton, "quite a number of cases would never exhibit to an ordinary observer any peculiarity indicating leprosy in more than one or two phases, as in a hand or foot. Some of these cases, what we may term localized cases, remain in much the same state—outwardly viewed—for ten years or more."

From what has been said, it is evident that in countries where leprosy is not endemic, but is only occasionally met with, its diagnosis is beset with greater difficulties. In such cases an inquiry into the history and antecedents of the patient may give a clew to the nature of the suspicious symptoms. Possible exposure, either by contact with a leper or by residence in a country where leprosy prevails, is, of course, a *sine qua non* of contagion.

The modes of infection in leprosy are so many and mysterious that the mere fact of residence in a leprous country, even without known contact with lepers, is sufficient presumptive proof of contagious exposure.

PROGNOSIS.

The experience of all ages is that leprosy is a practically incurable disease. With rare exceptions it progresses to a fatal termination. The prognosis in a given case is therefore unfavorable.

As regards the more or less rapid evolution of the disease, the prognosis is influenced by the constitutional vigor of the patient, expressed in the power of resistance of his tissues to the inroads of the bacilli, by climatic conditions and hygienic surroundings.

There is no infectious disease, of a necessarily fatal character, that is so protracted in its incubation, so mild in its initial manifestations, so prolonged in its exemption from serious accidents, and which grants its victim so long a lease of life as leprosy. Even after the characteristic evidences of the disease are manifest, the patient may live in comparative health for many years, with faculties unimpaired and capacity of usefulness and work practically undiminished. This is especially true of nerve leprosy.

In anæsthetic cases the entire symptomatology, for five or ten years, or longer, may be limited to a few erythematous patches and occasional neuritic pains. I have had under my observation three

patients with unmistakable signs of anæsthetic leprosy, two of twelve years' duration and one of seven years. In one case there has been a marked retrogression in the symptoms with apparent cure; in the other two the symptoms have remained practically stationary. It is a matter of common observation that in countries where the disease is endemic its course is much more rapid than when the patient is removed to a temperate climate where it does not prevail. Whether the abatement is due to the climate, the food, or the changed habits of living, there is commonly observed, for a time at least, an arrest or retrogression of the manifestations. Unfortunately this lull in the manifestations is, as a rule, not of long duration, and after a temporary truce the force of the disease reasserts itself and the patient finally succumbs. Lepers coming to this country, for example, almost invariably improve, for a time at least, and the disease pursues a milder and longer course.

As regards the duration of life, the prognosis is much more unfavorable in the tubercular than in the anæsthetic form. When there is a transition of one form into another the prognosis is more or less favorable, according as the prominent symptoms of one or the other gain the ascendency. As Leloir somewhat paradoxically phrases it, "the worst that can happen to a trophoneurotic leper is to become a tubercular leper. The best that can happen to a tubercular leper is to become a trophoneurotic leper."

Abortive Cases.—The occasional occurrence of a spontaneous cure of leprosy must be considered in connection with prognosis. There is a sufficient number of cases on record to prove that the disease may not only be arrested, but that all evidences of its active existence may definitely disappear. As compared with the vast number of cases that end fatally, the abortive cases are few in number, but in every country where leprosy prevails we have well-authenticated records of patients who have shown characteristic and unmistakable signs of the disease, experiencing a complete and permanent cessation of all manifestations. This exemption has been observed to continue for ten, twenty, thirty years, or longer, and the patients finally die of some other disease. This spontaneous cure may take place at any period of the disease. Most of the cases reported as cured are advanced in their evolution, and apparently the reparative process takes place after more or less damage to the tissues.

In a recent communication, Hansen, of Bergen, Norway, states that, of the 8,453 lepers who have been recorded in the leper statistics of Norway, from 1856 to 1895 there are one hundred and twenty-six cases tabulated as being cured. Hansen throws doubt upon the authenticity of cure in some of these cases.

Thin says: "If a patient loses all symptoms of tubercular leprosy and enjoys good health, but retains some slight symptoms of nerve leprosy of an unprogressive character, the case may be considered as much a case of cure as a case of phthisis in which all symptoms have become arrested, although the patient is left with a patch of fibroid tissue in his lung, in which doubtless the spores of tuberculosis are embedded." Arning reports that he has cognizance of a neurosis, in which the nerves were particularly affected, in which only one or more of the usual symptoms were present and when the condition of the patient would not have excited the slightest suspicion of leprosy in any other than a specialist. Such he regards as instances of abortive leprosy. Although such cases are well attested, many medical men, while admitting that the disease is permanently arrested, deny that the patients are cured, insisting that unless it can be proved by microscopical examination that no bacilli exist in any of the tissues of the body the case cannot be pronounced cured.

Even cases conforming to this crucial test are not wanting. Hallopeau reported to the Berlin Leprosy Congress the case of a young Haytien who had been affected with a severe form of nerve leprosy, and who succumbed to a pulmonary tuberculosis. A most careful bacteriological examination practised by M. Jeanselme after death demonstrated the complete absence of bacilli although they had been found abundantly some time before, showing that the patient was cured. There remained only the secondary stigmata of the disease.

Impey, who has had a large personal experience with leprosy in South Africa, is a strong believer in the curability of leprosy. He states that in anæsthetic leprosy the natural course of events is for the disease to expend itself, and if patients could only stand the terrible battle for life they would all become cured, but unfortunately the strain is too great and most patients die before the bacilli are able to work out their own destruction. He believes that the interstitial inflammation to which the nerves are subjected leads to a contraction and fibroid degeneration of their tissues, so that the sclerotic condition of the fibrous band or filament which represents the former nerve trunk presents an effectual bar to any further growth of the bacilli, and these, being deprived of nourishment, die. Likewise he believes that in tubercular leprosy the repeated attacks of congestion to which the tubercles are subjected in the course of the disease produce, in like manner, a sort of fibroid degeneration of tissues and this sclerotic tissue becomes firmer and denser in consistence and thus less able to support a mass of living organisms. He believes that we can, in cases not too far advanced, expedite this fibroid degeneration of the tissues and thus cure tubercular leprosy.

The commission appointed to investigate leprosy in the Cape of Good Hope reported (1895) that they believe leprosy is in some cases spontaneously arrested for longer or shorter periods, and in a small proportion of cases the arrest is permanent. There is no specific sign by which permanent arrest can be recognized, but the healing of ulcers, a quiescent state of the skin, a general appearance of good health, increase of weight, the absence of any indication of active disease, either external or internal, during two years may be regarded for all practicable purposes as an arrest of the disease.

I believe abortion of the disease occurs in the early stages much oftener than is generally supposed; leprosy presenting in this respect a striking analogy with tuberculosis. In all leprous countries the number of "suspects"—that is, persons who present suspicious but not positive unequivocal signs of the disease—is very large. Many such cases are classed as cases of leprophobia.

The natural process of cure is influenced by various conditions. In leprosy, as in other infectious diseases, morbid processes are determined largely by conditions of aptitude inherent in the individual. Thus the question of soil as well as of seed has to be considered. If the soil is unfavorable as a culture medium, the bacilli die of inanition. The only explanation of this spontaneous cure is that the tissues of these individuals are endowed with an unusual capacity of resistance to the germination and growth of the lepra bacilli. This capacity of resistance may be strengthened by change of climate and other measures to be considered in connection with hygiene and treatment.

TREATMENT.

The verdict of experience is that leprosy, in the vast majority of cases, is an incurable disease. Of the large number of remedies and methods of treatment employed none has been proved to possess a specific curative action upon the leprous process. In reviewing the literature of treatment we find that many drugs have been credited with exercising such action, but when this clinical testimony is analyzed it is found to be of the most conflicting and contradictory character.

In estimating the value of treatment certain possible sources of error should be considered. The study of the natural history of leprosy, abandoned to its own evolution and uninfluenced by treatment, shows that it does not pursue a progressive, uninterrupted course: the morbid process alternates between activity and repose; it often presents remissions sufficiently prolonged and complete to give deceptive indications of a cure. It may be formulated as a general law that recessions are the rule in leprosy, especially in the earlier stages.

If a remedy happens to be given when such a remission is about to occur, the observer is apt to attribute the spontaneous subsidence of symptoms to the treatment employed. On the other hand, if the treatment is instituted coincidently with an exacerbation or new outbreak, it is condemned as a failure. In the writer's opinion, the claims of most of the remedies which have been vaunted as "specifics" in leprosy are largely based upon *post hoc* conclusions as to results, which, rightfully interpreted, are mere coincidences. Again, all observation proves that under the sole influence of climate and hygienic treatment the general condition of leprous patients is notably improved.

In this country and Europe the therapeutic problem is complicated by the modifying influence of climate upon the course of the disease. It is a matter of observation that most lepers who come to this country get better for a time at least, with or without medication, and when treatment is employed it is difficult to differentiate between its effect and that of climate and improved modes of living. Thus in a case of pronounced tubercular leprosy referred to me some two years ago by a colleague in New York, the cutaneous manifestations entirely disappeared within a few months under the influence of large doses of Chaulmoogra oil internally, with daily baths and inunctions of Gurjun oil. In another patient referred to me several years ago by Dr. Besnier, of Paris, there has been an apparent cure from the use of phosphide of zinc and strychnine. It is difficult to determine what precise measure of curative influence should be ascribed to the drugs in these cases, since in another case under observation for two years there was an arrest of the symptoms under the influence of hot baths, massage, and general hygienic measures—no drugs whatever having been administered.

It is not intended to pass in review the innumerable drugs and methods of treatment employed in the treatment of leprosy. It would simply serve to illustrate the fact that the more intractable the disease the more numerous the remedies advocated for its treatment. The early methods of treatment possess an antiquarian rather than a practical interest. But as the history of leprosy is embraced within the scope of this article, it will be necessary, for the sake of completeness, to make some reference to the methods of treatment employed in ancient times.

In Mosaic times the treatment was altogether of a prophylactic character. In the Hebraic conception of the disease leprosy was regarded as a punishment for sin and an evidence of divine displeasure, and the only hope of cure was through divine intervention. The Levitical code gives no indications of the employment of any treatment directed to a cure of the disease.

At the time of Galen the treatment consisted in keeping the skin soft and moist with oily applications and suitable exercise. Swimming was particularly recommended as combining exercise with bathing.

Aretæus, whose graphic description of leprosy is quoted below in the section on History, lays down as the proper plan of treatment the practice of frequent and copious venesection, followed by the use of purgatives, baths, and inunction of fat, associated with a plain nutritious diet. The purgative most preferred was colocynth. Among the medicines he had experience of may be mentioned gum vernix, brassica, sideritis (ironwort) trefoil with wine and honey, shavings of elephants' teeth in wine. The flesh of vipers formed into pastils was also to be used to season the food. The compound medicine was made from levigated alcyonium, natron, sulphur vinum, costus, iris, and pepper, "these all to be mixed together in each case according to the power, but in proportionate quantities, and this compound to be sprinkled upon the body and rubbed in. For the callous protuberances of the face we are to rub in the ashes of vine branches mixed with the fat of wild beasts, as the lion, tiger, panther, bear, etc., or, if these are not at hand, of the fat of the barnacle goose; for like to the unlike, as the ape to the man, is most excellent. If the flesh be in a livid state, scarifications are to be previously made for the evacuation of the humors. Continued baths are ordered for the purpose of humectating the body. There is further recommended natural hot baths of a sulphurous nature and protracted residence in the waters and a sea voyage. White hellebore is recommended above all other things; for in power white hellebore resembles fire, and whatever fire accomplishes by burning still more does hellebore effect by penetrating internally—out of dyspnœa inducing freedom of breathing, out of paleness good color, and out of emaciation plumpness of flesh."

Etius follows the general plan of treatment described by Aretæus, adding that amongst the Indians it was customary to exhibit as "a medicine the urine of the ass, probably on account of its diuretic effects, and prescribe as an article of diet the flesh of the crocodile." Serpents and reptiles seem to have acquired their reputation, in this disease and other diseases in which the skin is affected, from their periodical exuviation of the cuticle and the magistral inference that their flesh, partaken by man, would enable him to throw off, by a similar process of exuviation, the sordid covering of morbid secretions and the scales which are apt to form in these diseases (Wilson).

Paulus Ægineta recommended practically the same treatment to be employed three or four times a year. In his list of medicines are

mentioned squills, cumin, calamint, hartshorn, theriac of salmis, and theriac of vipers. As a part of the hygienic treatment he recommended various forms of gymnastic exercise, particularly leaping, the body to be then anointed with the fat of some animal, as of the boar, wolf, goat, or bird, or with butter. After inunction the patient should take a bath and be rubbed with some stimulating juice or spirit, such as fenugreek, or gum ammoniac dissolved in vinegar. After the bath he is to be anointed with a solution of gum ammoniac and alum in white wine, or with some gently stimulating and aromatic oil, such as that of myrtle.

Rhazes, the Arabian physician, commences his treatment with emetics and reserves venesection for cases of severity or of long standing. He combines turbith with colocynth as a purgative and favors excitation of the skin by means of friction and hot baths, and further by the help of a liniment composed of onions and fennel, or of a lotion of strong acetic acid in which madder root has been for a time digested. If the powers of the constitution be reduced by the treatment, he recommends the use of good white wine (Wilson).

Daniellsen and Boeck give a summary of the treatment recommended by Schilling, towards the end of the eighteenth century. The diet during the first three months must be plain. At the commencement of the cure, so long as the "obstruction" lasts, milk must not be taken; later it may be allowed. Mercurials are abstained from because they always produce in lepers violent accidents and very often a dangerous diarrhœa. When signs of plethora are present, the patient must be well bled.

Warm baths should be employed, but carefully in advanced stages of the complaint, as being apt to occasion palpitations of the heart, convulsions, and fainting fits. He encourages exercise for the production of perspiration. As diluents he recommends barley water, gruel, and resolutive herbs, such as agrimony, ground ivy, fumitory, arbrotanun, veronica, etc., and tisanes, to which are sometimes added demulcents and purgatives, such as mallory, rhubarb, aniseed, pellitory, senna leaves. For six weeks the patient should drink eight pounds of these liquids daily, and as the state of the patient or the disease indicates he bleeds, purges, or adds tonic extracts to the preceding decoctions. After the above preparatory course of six weeks, the more powerful alteratives and sudorifics are ordered, especially soapwort, sarsaparilla, sassafras, china root, juniper, serpentary, scolopendrium, pareira brava, and other similar herbs. The greater the consumption of these decoctions, he claims, the more prompt and complete the cure. The body, however, he remarks, is apt to become weak under this treatment, and for this reason good and nour-

ishing food and good wines should be partaken of. He prohibits acids and spirits during the treatment, as being liable to cause febrile action. After having employed these remedies for about three months it is advantageous to practise bleeding and to take as much blood as the strength of the patient will allow. If the patient makes use of these curative means, he should avoid cold air, as it may happen that a critical perspiration is suppressed by the cold, causing severe diarrhœa.

The treatment should be pursued for some time after patients have recovered and be discontinued by degrees.

It will be perceived that many of the methods of treatment employed in ancient times, and even now in certain countries, seem more like incantations than rational procedures. In Amoy in China, for example, "the leper is enclosed in the carcass of a freshly eviscerated bullock, where he remains an hour or more." A snake, the flesh of a dead child, a cooked placenta (human) are among the edibles lauded by the Chinese for the cure of leprosy. In Fatshan, near Canton, according to Dr. McDonald, "lepers have a notion that eating the flesh of a dead child will cure them."

There is a belief prevalent in Canton and elsewhere that a leprous woman can rid herself of the disease by having connection with a healthy man. The woman by connection hopes to get rid of the disease by handing it over to the man. This curious practice is termed "selling off leprosy." Another curious belief prevailing in China is that sexual intercourse will act as a prophylactic against leprosy. Thus a woman having a leprous husband, but who herself shows no manifestations, will try to have a healthy man have connection with her, thereby lessening her chances of becoming infected at all.

Dr. Cantlie reports as the result of his investigations of leprosy in China (1) that no European records a single case of cure; (2) that no native drug has been found to be curative.

Simpson refers to a certain Christian Livingstone in the sixteenth century, who "took a reid cock, slew it, baked a bannock (cake) of the blood of it, and gave the same to a leper to eat." Michael Scott's cure is given as follows: "It ought to be known that the blood of dogs and of infants two years old and under, when diffused through a bath of heated water, dispels leprosy without a doubt" (Thin).

According to Erasmus Wilson, one of the specific remedies advocated in the treatment of elephantiasis was castration, under the impression that the stimulus given to the blood by the generative system was an excitant of the disease. Patients have relieved themselves of these glandular organs, but without any benefit whatever.

In the Middle Ages phlebotomy was recommended to expel the excess of melancholy, one of the four humors which instead of going to the spleen was, in leprosy, diffused throughout the entire body. In conjunction with bleeding the use of laxative medicines and fumigations, with nasal instillations to combat the nasal deformities, were employed. This treatment was, however, considered only adjuvant to the specific treatment which consisted in the administration of the flesh of vipers. These serpents were especially prepared and the flesh served up in various appetizing ways—in bouillon, with chicken, etc.; "in a word, it was to be absorbed in every possible way—in electuary, in distillation, in maceration." This mediæval practice has been mentioned only to show that the belief upon which it was based, viz., that there exists in the serpent tribe an "antivenom" which is antagonistic to the virus of leprosy, has prevailed in all ages, and it still survives at the present day. According to Ashmead, the antivenom treatment, which consists "in dissolving the snake *mamuslie* in wine and using the dissolution internally," has been known in Japan for a thousand years. In China from time immemorial the flesh of the *hungshe*, a very rare snake, dissolved in strong wine and taken internally has been regarded as a cure for leprosy.

In South America, especially among the Brazilians, there is a widespread faith in the saving efficacy of the bite of serpents against leprosy. Dr. Carreau, in 1892, reported the case of a leper bitten by a viper, in whom there was a remarkable disappearance of the tubercular lesions, which he attributed to the increase of hæmoglobin in the blood.

According to Dr. Laverde, lepers in Colombia cause themselves to be bitten by venomous serpents, scorpions, hornets, etc., but we possess only vague information as to the results of this barbaric therapeutics. It is certain that the result is often fatal, but when the patient survives there is a remarkable amelioration in the symptoms, and in some cases a permanent cure has been reported. The serpent *corral*, whose bite is rarely fatal, is most frequently selected for this hazardous procedure. This belief in the immunizing effect of snake poison forms the basis of the treatment of leprosy by the antivenom serum of Calmette and Fraser, which will be again referred to.

The treatment instituted by Daniellsen at the Lungegaards Hospital, Bergen, was based on the theory that in leprosy there is an excess of albumin and fibrin in the blood and that the abnormal constitution of this fluid could be best corrected by vegetable diet, sulphur baths, phosphoric acid, tartrate of antimony, iodide of potassium, iodide of iron, chlorine, and remedies of this class. Arsenic was used sparingly and in small doses. Mercury was regarded as not only useless

but injurious. In some cases venesection was employed. In the local treatment of the tubercles acid nitrate of mercury or solution of caustic potash was used for their destruction, or recourse was had to caustic or sulphuretted baths. Daniellsen also employed syphilization on the theory that the syphilitic poison might prove superior to that of leprosy and the production of a syphilitic dyscrasia might transform or annihilate that of leprosy; the result was that the syphilitic process went on while the leprosy remained unchanged. Iodide of potassium was extensively experimented with by Daniellsen with good results in the tubercular form. Leprous patients were soon found to be peculiarly susceptible to its irritant effects upon the skin, and, according to Daniellsen, it affects them both as a powerful poison and a means of cure. He found the salicylate of sodium effective and useful in both forms of leprosy. In the tubercular form the newly formed nodules disappear, but old nodules of long standing were not apparently affected. The external application of a concentrated solution caused the nodules to disappear partially, but when the application was discontinued the nodules again became apparent. Chaulmoogra oil was used with the most unsatisfactory results, as it seemed to bring out severe eruptions of nodules. The use of salicylate of mercury, though this was borne better than other mercurial preparations, was followed by no improvement.

Daniellsen summarizes the results of his long and extensive experience as follows: "I have employed in my services all the medicaments which have been so much vaunted in the treatment of leprosy—all, from the iodide of potassium to that of chaulmoogra, gurjun oil, creosote, etc. They have been sent to me from all countries. I have oftentimes had moments of hope, but I have been forced to the conviction, which I must again repeat, I do not know of a medicament which cures leprosy."

Oil of Cashew Nut (*Anacardium occidentale*).—A plan of treatment which attracted considerable attention some thirty years ago was that known by the name of its author as the Beauperthuy treatment. In addition to a careful diet, daily baths, etc., he sought to correct the dyscrasia by the administration of the bichloride of mercury in small doses. The external applications were liniments to cure the eczematous and other eruptions, and for the active removal of the tubercles a strong solution of nitrate of silver and copper formed by dissolving silver coin in concentrated nitric acid and diluting with an equal bulk of distilled water; but principally the oil of cashew nut (*anacardium occidentale*) was employed for this purpose. The oil of cashew was applied with a sponge, or a needle dipped into it would be used to puncture a tubercle in order to set up suppuration.

This treatment did not fulfil the high expectations which had been formed of its curative value. It was tried in India, Norway, and elsewhere and abandoned. The cashew nut is still extensively employed in the local treatment of leprous nodules.

Hydrocotyle asiatica was introduced by Dr. Brileau, of Mauritius, himself a leper, who claimed to have cured himself and many others with this drug. According to Dr. Lepine, the properties of the plant are due to an active principle which he terms vellarine. It appears to have a peculiar action on the capillaries of the mucous surfaces and upon the skin; it causes first a sensation of heat in the stomach and at the same time a prickling in the extremities and then over the skin of the whole body, followed by increased transpiration, etc. From its stimulating effect on the circulation it is considered to be especially indicated in the anæsthetic form of the disease.

The three vegetable remedies which have been most highly vaunted as specifics and which have been generally held in highest repute are chaulmoogra oil and gurjun oil and Hoang-nan.

Chaulmoogra oil, expressed from the seeds of the *Gynocardia odorata*, which probably enjoys the highest degree of professional confidence, was first used by Le Page, of Calcutta, in the treatment of leprosy. It is given in doses varying from five to eighty drops three times a day, in emulsion or in capsules. The best results are obtained when large doses, two hundred to three hundred minims daily, are administered. Unfortunately, the oil is very irritant to many stomachs; some cannot tolerate it even in the smallest doses. I have a patient in whom a dose of two or three minims invariably causes anorexia, disagreeable eructations, and sometimes vomiting. In cases in which the oil is not well supported, Vidal has recommended its active principle, gynocardic acid, in the form of gynocardate of magnesium or sodium, given in capsules, containing 20 to 30 cgm. each. Of these, ten to twenty may be taken each day. Externally chaulmoogra oil may be used in the proportion of one part of the oil to five or fifteen parts of olive or cocoanut oil, or in the form of an ointment of gynocardic acid. Under the prolonged use of chaulmoogra oil it is claimed that there is a notable amelioration of the symptoms —the skin becomes soft and supple, discolorations clear up, leprous nodules undergo involution, ulcers heal, disorders of sensibility are corrected, the general nutrition improves, and the patients gain in weight. Numerous physicians have published cases in which decided benefit was derived from the use of this drug. It seems to have the best effect in tubercular cases. Beaven Rake, Carter, and many physicians who have largely experimented with the drug, testify that under its use the nodules in the skin subside and

the sensory nerves more or less regain their function. Other observers, after an extensive trial, have not been impressed with the value of this remedy.

Gurjun oil, derived from the *Dipterocarpus turbinatus,* first recommended by Dr. Dougall, has a high repute in India. It may be given in an emulsion, equal parts of the oil and lime water, the dose of which is from one to four drachms. As a local application it may be used in the proportion of one part of the oil to three parts of lime water or olive oil. To secure the best results the oil should be rubbed in thoroughly, two hours each day being employed in the process, after which a bath should be taken, and the inunction repeated every day. Dr. Hillis states that the gurjun oil seems to exert a specific action on the sweat glands, evidenced by the increased perspiration and return of sensation in anæsthetic areas, and that it is a most valuable agent in all forms of leprosy. He further claims that by the use of the gurjun oil in suitable cases the disease may be arrested, and that in a few instances there has been no return of the disease for over two years; but it may, nevertheless, be premature to say that a cure has taken place. In a later report he says: "In gurjun oil we appear to have a most valuable medicine for the treatment of leprosy in all its forms—one capable of retarding the ravages of the disease and in some cases of apparently curing it."

In India a number of medical officers, Dr. Neve and others, report that patients improved under the action of gurjun oil, and that ulcers and cracks of the integument particularly healed under its application.

On the other hand, many other observers have tried it and found it of no particular value. Bidenkap states that he has tried it without result, although the frictions connected with its use seem to have a favorable influence upon the affections of the cutaneous nerves. Beaven Rake considers that the value of gurjun oil has been greatly overrated, although he concedes that its external application is of use in removing scabs or desquamation. Vandyke Carter also depreciates its value, declaring that the results are disappointing.

Hoang-nan (*Strychnos gaultheriana*) is a remedy which has been highly extolled in China and other countries where leprosy prevails. It comes in the form of a reddish powder from the bark of a tree found in the forests of Annam. This is made up in the form of pills with gluten. During its administration all alcoholic drinks are suppressed and a simple diet, preferably a milk diet, is recommended. The remedy should be used with care, as it is claimed its injudicious use may be followed by tetanoid symptoms. I have known of one case in the leper settlement of Molokai of advanced nerve leprosy in which the anæsthetic symptoms cleared up under the use of Hoang-nan,

and the improvement has continued for several years. The patient regards himself as practically cured. In other cases the beneficial effects of the remedy have been pronounced and positive.

Strychnine, the active principle of nux vomica, is probably closely allied in its action to Hoang-nan and has been largely employed, and with excellent results, in the treatment of the anæsthetic form of leprosy in this country.

Ichthyol.—Some ten years ago Unna claimed to have cured two cases by the internal administration of ammonium sulphoichthyolate and the external use of certain reducing agents, as chrysarobin, resorcin, pyrogallol, salicylic acid, etc. The reducing agents he asserted to be most effective when used in a weak strength, in five- to ten-per-cent. ointments. In some cases strong ointments of chrysarobin or plaster mulls containing forty parts each of creosote and salicylic acid were applied to the leprous nodules with a view of exciting an inflammation of the skin and effecting an elimination of the bacilli. The claim that the patients were cured was premature, as both died of the disease, one of them within twelve months. A more extensive clinical experience by others, instead of confirming the value of this method of treatment, has demonstrated it to be a failure.

Salol, which has been highly recommended by certain observers, has been found utterly useless by others. The value of salol was highly extolled by Lutz. He claimed that in large doses the leprous fever is arrested and the eruption retrogresses with the healing of the ulcers; anæsthetic patches again become sensitive, and the scaly, shining appearance of the skin gives way to a moist, healthier look. On the other hand, Dr. Cook, superintendent of the Government Leper Hospital of Madras, after an extensive experience with this drug, declares that "salol, in my opinion, is of no therapeutic value —in fact, I consider it a decided failure."

Salicylicate of sodium and salicylic acid were extensively employed by Daniellsen and Köbner, who state that these remedies are effective in both forms of leprosy. In the tubercular form the fever is lessened, the eruptive period shortened, and some nodules disappear. The sodium salicylate was given in doses of from 3 ss. to 3 iss. (2 to 6 gm.) daily. Bidenkap has seen more harm than good result from the use of salicylate preparations.

Creosote and Carbolic Acid.—Langerhans and Perez claim to have had excellent results from the internal administration of creosote. Bidenkap and others found in their experience creosote and carbolic acid powerless.

Europhen.—Dr. Goldschmidt, of Madeira, claims to have cured incipient tubercular leprosy by the application of europhen oil

(iodine in a nascent state). In one case, after six years there had been no return of the disease. Alvarez, of Honolulu, tried the europhen treatment with "negative results." Havelburg, of Rio Janeiro, has used europhen, formalin, and nosophen internally and locally as salves or injected into tumors, as he declares, without any real effect (Ashmead).

Crude Petroleum.—Kalindero has been most favorably impressed with the use of crude petroleum from which he has observed a marked amelioration of the leprous symptoms.

Chlorate of Potassium.—From the well-known action of this drug in causing a rapid increase of hæmoglobin in the blood, Dr. Carreau, of Guadeloupe, used it in large doses, gr. cl. to clxxx. He reports remarkable results from its employment, shown in the disappearance of the nodules as well as in the thickening of the integument and restoration of sensibility. Beaven Rake experimented with chlorate of potassium, but with unsatisfactory results. As the bacilli are not found in the blood it is difficult to see how a modification in the composition of the blood affects the life of these organisms.

Airol (oxyiodogallate of bismuth).—On account of the well-known microbicidal action of this agent, Fornara employed it in the treatment of leprosy. He injected it in emulsion (one-tenth airol with one-third glycerin or olive oil previously boiled) in tubercles, plaques, swellings, and anæsthetic areas, graduating the dose from one drop to a Pravaz syringeful, according to the extent of the lesions. If the eyes were attacked, it was instilled several times a day into the conjunctival sac. If the nose and throat were involved, the powdered drug was snuffed up like tobacco, the object being to saturate the tissues with airol. In some cases chaulmoogra oil was also used internally and an ointment of the oil externally. Fornara reports seven cases in which there was either a cure or a marked amelioration of all the symptoms.

Formalin has been extensively employed in the treatment of leprosy on account of its germicidal properties. It has been used externally as a caustic and in frictions rubbed up with lanolin, and has also been injected into the tubercles. When it is thus employed the tumor hardens as if tanned and is eliminated. It is not regarded, however, as superior to other caustics for the destruction of the pathological formations of leprosy.

Pyoktanin is another bactericide which has been experimented with in the treatment of leprosy. The tumors into which it was injected assumed a blue color, small abscesses were formed, and the necrotic masses were eliminated, but it was found to have no effect on the general manifestations or course of the disease.

Thyroid extract is a remedy which has been experimented with on the supposition that from its effect in reducing myxœdematous infiltrations it might be useful in the diffuse and œdematous infiltrations of leprosy. It has been tried extensively in South America and by Alvarez, of Honolulu, who claims that it has a remarkable efficacy in dissipating the œdematous swellings of leprosy. Its continued use does not, however, modify the general condition of the patient.

Tuberculin.—The treatment of leprosy by injections of tuberculin, which was introduced some years ago, is mentioned only to be condemned. It was extensively experimented with, but the results have been invariably disappointing. The intense vascular disturbance produced by the injections is so marked as not only to render more prominent existing leprous infiltrations, but to cause new manifestations of the disease in parts previously exempt. In a case reported by Abraham, after the third injection two large swellings resembling nodes appeared, one in front of each tibia; several tubercles made their appearance on the face, forearms, and elsewhere, and some of the older tuberosities became more swollen. In a case of mixed leprosy under my observation there was a marked aggravation of all the eruptive features with the development of new foci of the disease. In another of my cases (anæsthetic) there was no change in the condition of the patient beyond the febrile reactionary effects. The concurrent testimony of almost all observers is to the effect that the action of tuberculin is positively pernicious in determining the development of new foci of the disease.

Injections of Bovinine, Meat Juice, etc.—J. A. Voorthuis reports experiments with Unna's method of treatment of lepra which was employed in the cases of four Chinese coolies in Deli (Sumatra); this consisted in intravenous injections of Valentine's meat juice thinned with an equal part of artificial serum, 0.2 to 1 c.c. every two days. In all cases there was a bettering of the general condition with reddening and swelling of the nodules, which then softened and were resorbed or were emptied by incision. This method of treatment is based upon the ground that the muscular tissue which is dissolved in meat juice is the only particular substance of the body which is immune to the lepra bacilli.

Intramuscular Injections of Perchloride of Mercury.—Although mercury has been commonly credited with exercising a positively injurious action in leprosy, exception being, perhaps, made for cases in which there is a combination with syphilis, Crocker reports five cases in which a striking improvement was manifest after intramuscular injections of perchloride of mercury. He is positive that the improvement was not a matter of chance, but was the direct

effect of the treatment. The dose is one-fourth of a grain, which is injected twice a week. Crocker notes as a curious circumstance that none of the patients suffered from salivation, nor does the drug appear to have had a depressing effect when used twice a week for many months. One phenomenon of special interest was observed in all cases, viz., the appearance in different parts of the limbs of hard, pea-sized nodules, sometimes cutaneous, sometimes subcutaneously seated, which were unlike the leprosy nodules. They were tender at first, later they became painless; some persisted for months, others disappeared in a few weeks or days.

Formamide of Mercury.—Hasland, of Copenhagen, has reported remarkable results in a case of tubercular leprosy from injections of formamide of mercury. One injection of 1 cgm. of the drug was given daily, except when the treatment was interrupted temporarily by intercurrent diarrhœa, until fifty-two injections had been made. The patient received six times daily a tablespoonful of a solution of salicylate of sodium (10 : 300). He also received later oleum gynocardii, beginning with five-drop doses three times daily and increasing. Externally an ointment of ichthyol-salicylated vaseline was used. The ulcerations were cured, the tubercles diminished in number, and the mucous membranes of the nose and pharynx became entirely smooth. Later there was a relapse. The same patient was seen later by Ehlers, when tubercles, spots, ulcerations, and swelling of the ulnar nerve were found.

Ehlers, of Copenhagen, has tried the injections of soluble salts of mercury in many cases. The treatment is followed by immediate good results, but it does not prevent recurrences.

Antivenene Treatment.—Dr. Dyer, of New Orleans, impressed with some respect for the popular superstition among the natives of South America and the West Indies, that the bite of a venomous snake would cure leprosy, experimented with Calmette's antivenene in five cases of leprosy. The injections were made every other day at first, subsequently every day. The dose varied from 1 to 11 c.c. The total number of injections in each case varied from ten to forty-two. The regions selected for the injections were the gluteal or interscapular; in some instances the injections were made in the nodular lesions themselves. Wherever this was done the lesions injected disappeared. In four out of the five cases treated by antivenene there was marked improvement; in one there was a practical disappearance of the lesion present and of other evidences of the disease. "Cold sweats" was the most characteristic feature of the constitutional reaction following the injections.

Erysipelas and its Toxins.—Reference has already been made to

the observation that an intercurrent attack of erysipelas has a markedly modifying effect upon the manifestations of leprosy. So long ago as 1882 Campana inoculated two leper patients with the products of erysipelas. The lepers were not cured, but all the other patients in the ward contracted erysipelas. In 1891 Havelburg, of Rio Janeiro, tried injections of cultures of the streptococci of erysipelas. He found that the reaction, both local and general, was so violent that the experiments had to be discontinued. A serum obtained from animals immunized against erysipelas, prepared by Emmerich and Scholl of Berlin, was then substituted for the erysipelas cultures and tried in the cases of five lepers. The injections were made two or three times a week in the lepromata and circumjacent tissues, and each patient received from fourteen to eighteen injections. The effects were variable. Sometimes no local reaction whatever was produced; at other times phlegmons and abscesses formed precisely as after injections of pyoktanin, alcohol, or phenic acid. The treatment was discontinued on account of the unsatisfactory results.

Quite recently H. D. Chapin, of New York, has published the results of his treatment of four lepers in the City Almshouse by the injections of the mixed unfiltered toxins of the streptococcus of erysipelas and the bacillus prodigiosus made from cultures grown together in bouillon. The injections, beginning with one minim and gradually increasing to twenty-two minims, were continued almost daily for about two months. The injections produced the characteristic reactions and temperature changes, but had no effect upon the course of the disease.

Impey thinks that the good effects of an attack of erysipelas are due not to an antagonism of germs, but to the intense inflammation which brings about sufficient degeneration of the tissues to bar the further growth of the bacilli if it does not actually cause their destruction.

Alvarez, of Honolulu, has been experimenting with injections of cultures of the bacillus prodigiosus, but without curative result.

Serum Therapy.—Among the more recent methods of treatment which were presented and discussed before the Berlin Leprosy Congress may be mentioned the serum treatment of Carrasquilla with its numerous modifications by other experimenters. This method of treatment was invested with an especial interest as the latest and perhaps most promising therapeutic novelty. To Dr. Juan de D. Carrasquilla, of Bogota, Colombia, is due the credit of introducing the serum treatment of leprosy. His serum is prepared as follows: A leper in the active stage of the disease is bled, preferably during one of the periodical exacerbations; the blood is allowed to

coagulate, and the clear serum is drawn off. This serum is preserved with camphor and injected into a horse; three injections of 30 c.c. each being given at intervals of ten days. The horse is bled ten days after the last injection, after which Carrasquilla repeats the same process, obtaining at the end of each month a progressively more active serum. He begins by injecting into a leper 1 to 3 c.c. of the camphorated horse serum, gradually increasing the dose to 5 c.c., and injecting on alternate days.

He claims that in the subjects of his experiments improvement began in a week and was marked at the end of a month. He describes in detail a number of cures, over two hundred in all, and sums up the benefit of his treatment as follows: (1) Reëstablishment of sensation; (2) decoloration of blotches; (3) disappearance of œdematous tubercles; (4) healing of ulcerations; (5) shrinking of the distorted face. He maintains that the morbid process ceases after the first injection.

J. Olaya Laverde, of Socorro, one of the most enthusiastic advocates of the employment of serum in leprosy, has introduced certain modifications in the method of its preparation. He injects asses and goats with the morbid products of leprosy, and claims that he thus obtains a more active serum. He collects 15 gm. of blood, 25 gm. of lepromes which he triturates and adds 20 gm. of sterilized water, 40 c.c. of which is at once injected under the skin of a goat in the scapular or pectoral region. The animal usually suffers some febrile reaction lasting several hours. At the end of six or eight days the animal is bled and the serum is injected into the patient, the quantity varying from 5 to 20 c.c. The injection produces a febrile reaction more or less marked, sometimes headache and wandering pains in the lumbar or epigastric region, followed by an abundant transpiration.

Laverde has treated about sixty patients, many of them receiving from thirty-five to forty injections. He reports that the therapeutic results are most satisfactory, the infiltrations are resorbed, the thickenings clear up, the spots and pigmentations gradually fade out, the tubercles are either absorbed or break down and disappear by suppuration. The anæsthesia, pain, mucular paresis, and other neuritic symptoms are effaced, the patients regain the use of their limbs, etc.

On the other hand, Putnam, of Colombia, has tried the Carrasquilla treatment on forty lepers without success.

The Carrasquilla serum was distributed to leprologists for experiment in various countries, almost all of whom reported adversely at the meeting of the Berlin Leprosy Congress.

Hallopeau treated six cases in the Hôpital St. Louis with negative results. Besnier regarded it as generally unsatisfactory, as it produced no sensible modification of the disease.

Alvarez, of Honolulu, employed the treatment in fourteen cases, two of which were improved. He often observed new eruptions during the progress of the treatment, contrary to the statement of Carrasquilla, that after the first injection no new manifestations of the disease appear. He observed in two cases severe attacks of asphyxia after the injections.

Barillon, Dehio, Brieger, Arning, Doutrelepont, and others observed no favorable result whatever from the serum of Carrasquilla, but many times febrile reactions more or less intense.

A. Grünfeld employed an antileprous serum prepared at the laboratory of E. Merck, of Darmstadt, after the method described by Carrasquilla. This serum was injected into two lepers for six months. Dr. Grünfeld reported a notable amelioration of the general condition of his patients after the use of the serum. He recommended as a necessary condition of success that the treatment should be continued for a long time.

Herman procured the clear serum from leprous nodules by clamping, incising, and pressing out the exudation. This leprosy exudate was injected into a horse every week until he received ten injections. The horse was bled and the serum collected in the usual way. This serum was used in five or six cases. One patient was thought to be improved, but the results could by no means be considered as brilliant.

Atherstone and Sinclair Black, of the Robben Island Asylum, made a number of experiments with the Carrasquilla serum and the "antileprotic serum" of Herman and at the same time made control experiments by injections in other cases of horse serum, asses' serum, and the serum of patients with arrested leprosy. The results were far from establishing the specific curative action of any of these serums upon the leprous process. The injections were followed by febrile reactions, headache, and profuse perspiration, but "the leprotic process suffered no arrest of a marked character."

Independent of the constitutional reactions the serum injections are often attended with the formation of painful swellings and abscesses at the points of injection. "The skin after numerous injections becomes tender, and the abscesses are very apt to cause great distress to the patient, even when the strictest antiseptic precautions have been employed to prevent such a result."

The weak point in the serum therapy of leprosy, and which *a priori* would disqualify it from a scientific standpoint, is that neither

the Carrasquilla serum nor any of the antileprotic serums can be considered in any sense as representing a leprous serum.

The bacilli lepræ are not habitually found in the blood. Their presence in the blood current during an attack of leprotic fever is purely hypothetical; therefore in injecting the blood of a leper into an animal there is no probability that leprous germs are conveyed. Even when a portion of lepromatous tissue or the serous exudate from a tubercle containing bacilli is introduced there is no assurance that the bacilli can be cultivated in the blood current of the animal, as all experiments prove that animals are refractory.

Even assuming that a culture of lepra bacilli may be made outside the human body and an animal be found susceptible to this culture inoculation, it is questionable whether the serum obtained from this animal would cure leprosy. In the case of tuberculin, all the ideal conditions for the production of a perfect serum have been fulfilled, yet the results of the practical employment of this substance in the treatment of tuberculosis have been most disappointing.

It is difficult to reconcile the enthusiastic testimony of Carrasquilla and Laverde in favor of the beneficial effects of serum therapy with the almost universal condemnation it has received at the hands of other experimenters.

The same may be said of the clinical testimony as to the therapeutic value of a long list of remedies which are highly praised by some observers, and by others equally competent are condemned as useless or harmful. We thus perceive that among men who have had the largest opportunities for experiment there is a most unfortunate lack of unanimity as to the value of any of these various remedies, exception being possibly made for chaulmoogra and gurjun oil and agents of the Strychnos family.

While many of the remedies and methods of treatment of leprosy are purely empirical and without rational basis, it will be perceived that most of the agents of recent introduction have been employed on account of their bactericidal properties. It is evident, however, from the position of the bacilli in the deeper tissues that no germicidal agent can be brought into direct contact with the pathogenic organisms; and even if this were possible, there is no agent capable of destroying the bacilli without destroying the tissues containing them. The true indication of rational treatment would seem to be to sterilize the tissues so as to render them unsuitable for the growth and multiplication of the bacilli.

Many of the agents employed (chaulmoogra, gurjun oil, and many other remedies), it is claimed, so modify the economy as to render the tissues sterile and inapt for the nutrition of the bacilli.

From my own observation and experience I am inclined to the belief that chaulmoogra oil exercises a more directly curative action upon the manifestations of tubercular leprosy than any of the numerous drugs which have been recommended, although I by no means share the enthusiastic faith of those who claim that it exerts the same specific action in leprosy that mercury does in syphilis. In order to secure the full measure of its therápeutic efficacy it should be given in large doses, even as high as from one to four drachms per day. The oil does not seem to be toxic, but it possesses the unfortunate disadvantage of being extremely nauseating, so that many patients cannot take it, even in small doses, without experiencing disagreeable eructations and sometimes nausea and vomiting. The administration of the oil in capsules, followed by a drink of tea or a little rum, renders the stomach more tolerant of its presence.

In other cases recourse may be had to its active medicinal principle, gynocardic acid, combined with sodium or magnesium. I have found the gynocardate of magnesium much better tolerated than the pure oil and apparently equally effective.

Hot baths and inunctions of gurjun oil with massage will be found useful in both forms of leprosy. Hoang-nan is a remedy which finds its special application in cases of the anæsthetic type. As this is not an easily procurable drug in this country, I have treated most anæsthetic cases with preparations of strychnine, which may be used either alone or advantageously combined with phosphorus, iron, and other nerve and ferruginous tonics.

Electricity is an agent which has proven in my experience especially serviceable in restoring impaired or lost sensibility in anæsthetic areas. The condition of success is, however, that it should be used faithfully and for a long period.

The case of which a short history is given on page 513 continued under my observation several years, and the results of the treatment were so satisfactory as to justify its description.

The patient was first given chaulmoogra oil in capsules, but on account of the gastric and intestinal irritation occasioned by the drug its use for any continued length of time was impossible. The gynocardate of magnesium was substituted, but even this occasioned some gastric irritation, though much less pronounced than when the pure oil was used. For some time the patient received injections of tuberculin; there was some constitutional reaction of a very pronounced character, but the influence of the remedy upon the disease seemed to be absolutely nil. Finally the patient was placed upon the phosphide of zinc and strychnine, the use of which was continued with intermissions for two or three years.

Electricity was first employed in order to restore, if possible, the sensation in the anæsthetic patch over the instep. The result was exceedingly slow, but quite satisfactory. The normal sensation returned in the course of two years. The electricity was also applied along the course of the sciatic and ulnar nerves, which had shown evidence of commencing degeneration manifest in a tendency of the limbs to go to sleep, with more or less numbness and loss of sensibility of the hands and feet.

The patient continued the use of the electricity for three or four years. At the last examination two years ago it was found that the hyperchromatic margin of the patch over the instep was broken and disappearing at certain points. The other macular lesions were also in process of disappearance. The patient wrote recently (October, 1898) that she thought she was entirely well of her trouble.

As before intimated, patients coming to this country may show signs of improvement, for a time at least, with or without treatment, and it is sometimes difficult to assign the true measure of therapeutic efficacy to the drugs employed. It is to be observed, however, that although leprosy seems to pursue a milder and a longer course in this country, it almost invariably progresses to a fatal termination, and due credit should be given to any treatment which arrests its further progress.

One explanation of the conflicting character of this clinical testimony is found in the nature of the disease. Leprosy always runs a protracted but exceedingly variable course, periods of active invasion being followed by periods of latency and even improvement, and when retrogression of the symptoms occurs it is difficult to estimate the part contributed by treatment to this result.

Again, in experimenting with a new remedy the physician is apt to select such cases as are not far advanced and in fairly good condition. These patients are commonly placed in good hygienic conditions, supplied with better food, and are the objects of daily individual attention. It is well known that leprous patients often have periods of great improvement and even apparent arrest of the disease under the influence of hygienic treatment alone; hence there may be a fallacious deduction in ascribing the improvement to the specific action of the remedy employed.

Another reason of this contradictory testimony as to the value of a special mode of treatment is that one observer may find it beneficial after prolonged use, while another condemns it upon an insufficient test. The more we study leprosy the more we are convinced of the fact that the essential condition of successful treatment is that it should be perseveringly continued for months and years. At one

time a six weeks' and later a six months' treatment of syphilis was regarded as quite sufficient, but at the present we recognize that the treatment should be prolonged for a period of years corresponding to the natural life term of the malady. Doubtless one reason of the almost uniform failure of all treatment instituted for leprosy is that it is not sufficiently prolonged, the recession of symptoms being taken both by the physician and patient as an indication of cure and a signal for the cessation of treatment.

In most leprous countries it is difficult to subject the patient to a course of treatment sufficiently prolonged and energetically carried out to judge of its value. In leper hospitals and communities most patients are impressed with the futility of all hopes of cure and soon tire of systematic treatment. In the leper settlement of Molokai the resident physician has given it as the result of his experience that "the scientific treatment of leprosy cannot be carried out because not more than ten per cent. of the patients will continue it for six months."

The "Japanese treatment," which consists of a system of baths and tonics, has been more thoroughly tried in the Molokai settlement than any other method. Dr. Gotto was employed by the Hawaiian Government, and special baths were especially fitted up to enable him to apply his method. The treatment has fallen into disfavor and been practically abandoned. In a letter from Mr. Dutton the effects of this treatment are incidentally referred to as follows: "The Japanese so-called 'remedies' act as a check. For some years the checking process continues if the rules as to medication, baths, etc., are closely followed. The pains are lessened at times, but the body seems to become weaker, and I doubt if the final result is of great benefit. We still use the hot baths, but not so frequently as the Japanese system requires—three times a week instead of three times a day. The effects are good in inducing cleanliness and also in causing perspiration, if care is taken not to catch cold."

In addition to the numerous remedies which have been employed on the assumption that they exerted a more or less special action upon the leprous process there are many drugs which have been used in the symptomatic treatment of the disease, and often with good effect, such as quinine, arsenic, opium, antipyrin, and bromide of potassium. The latter drug, according to Besnier, is exceedingly useful as a nervine. Tonics, iron, cod-liver oil, and reconstituent remedies generally are found most serviceable in improving the tone of the system and counteracting the anæmic condition so commonly present in this disease.

The visceral complications of leprosy which ordinarily supervene

at a more advanced stage, such as bronchial, renal, and gastrointestinal disorders, should be treated symptomatically. Paracentesis is occasionally necessary for the dropsy which accompanies the renal disease so common in leprosy. Beaven Rake found the kidneys diseased in twenty-five per cent. of the autopsies on lepers.

Local Treatment.

In the systematic treatment of leprosy local applications have proven a most valuable adjunct. Chaulmoogra and gurjun oils are not only applied locally in conjunction with the internal administration of these drugs, but in many cases in which the latter occasions much gastric irritation their use by inunction alone has been found to exercise quite a beneficial influence in causing to disappear the nodular lesions as well as the diffused infiltrations of the integument. The admixture of these oils with vaseline or lanolin in variable proportions has been recommended when they are to be applied over a large surface.

The use of baths followed by inunctions with oils or fats seems to have been practised in all ages. The ancients attributed especial virtues to the fats of certain animals, as the lion, the bear, the boar, and the panther.

One condition of the good effects of oily preparations is that they should be thoroughly rubbed in and their use continued for a long period. It has been said that to be cured of leprosy one must live in grease for months and years. The external use of linseed oil, cacao butter, or cod-liver oil would probably be followed by equally good results as have been claimed from the use of chaulmoogra or gurjun oil; the chief benefit, in my opinion, being derived from the two hours' daily rubbing required in their inunction.

The local treatment of the tubercles and ulcers, necrosed bones, and other individual lesions of leprosy should be conducted on general surgical principles. In allaying inflammation, removing necrosed tissues, and promoting the healing process the resources of modern aseptic surgery may be most advantageously employed. The existence of leprosy can scarcely be considered a contraindication to any required operation, as the tissues heal with remarkable facility owing, as has been suggested, to the excess of fibrin in the blood. By Daniellsen and Boeck the proportion of fibrin in the blood of lepers has been estimated from 0.22 to 0.6 per cent. Beaven Rake found in fifty carefully conducted analyses that the percentage ranged from 0.12 to 1.87, the average being 0.76, which is a marked excess over the normal proportion, 0.2 per cent. He attributed the rapid

healing of incisions in lepers to the very rapid clotting which takes place in their blood. Tubercles may be excised, ulcers may be scraped, deep incisions made, necrosed bones removed, and amputations performed with the certainty of more or less prompt cicatrization.

Dressings.—A variety of dressings, both wet and dry, have been employed for the healing of the ulcerations and for their aseptic properties. Lotions of the sulphate of copper (gr. iv. to ʒ i.), of carbolic acid (1 : 40), of corrosive sublimate (1 : 2,000 or 1 : 3,000) have been employed. A lotion of the permanganate of potassium is probably the most extensively used. Many of the powders which are used in the treatment of ordinary ulcerations have been employed for their aseptic and presumed germicidal properties, such as iodoform, iodol, aristol, europhen, saliphen, nosophen, airol, etc. Creolin was regarded by Beaven Rake as a most excellent stimulant for indolent leprous ulcers. Pure creolin was used by him as a caustic to prevent recurrence of leprous tubercles after excision.

Ointments are most in favor with leprous patients, as they do not dry, necessitating frequent application, and do not form crusts. Iodoform ointment is declared by many to be the most useful of external applications. It not only acts beneficially upon the open surfaces, but it masks by its penetrating odor the still more disagreeable fœtor which arises from the leprous discharges.

Reference has already been made to the local use of ichthyol, chrysarobin, resorcin, pyrogallol, and other reducing agents in the systematic treatment of leprosy. I have used these agents in a number of cases without being able to satisfy myself that they were productive of any benefit. In estimating the value of such measures, it is well to bear in mind the spontaneous tendency of the patches to fade with a return of normal sensation and function. In one case I noticed the disappearance of patches under the application of caustic pyrozone, and in another under a strong application of menthol which was continuously employed for a lengthened period.

Surgical measures play a much more important rôle in the treatment of anæsthetic leprosy than of the tubercular form. Of 1,996 operations performed within six years at the Trinidad Asylum, Beaven Rake states that 1,489 were done on anæsthetic males and 88 on anæsthetic females. Among tubercular cases there were 83 operations on males and 26 on females. In cases of mixed leprosy the operations on males numbered 300 and those on females 10. The greater preponderance of operations on males is explained by the fact that they are more exposed from their outdoor work to injuries which result in ulcers and necroses.

Removal of Tubercles by Excision or Destructive Cauterization.—The obliteration of tubercles has long been recognized as a correct surgical procedure, especially in the early stages and when they are localized on the face and extremities. Danielsen was accustomed to effect this by destructive cauterization with caustic potash or the acid nitrate of mercury; nitric, carbolic, salicylic, pyrogallic acids, and various caustics have been employed for this purpose. Destruction of the tubercles has also been effected by the injection into their substance of various irritant and escharotic substances, as oleum anacardii, pyoktanin, alcohol, carbolic acid, etc. The inflammatory reaction thus induced proceeds to suppuration, the breaking down of the nodules, and the discharge of their contents, after which cicatrization takes place.

A very satisfactory method of destroying the nodules is by the use of the thermocautery, either with or without preliminary removal of the mass with the curette. This procedure is preferred by many surgeons, as the operation is easily done, and it gives a better cosmetic result in the shape of a smooth cicatrix. In using potential caustics the depth and extent of the destructive action cannot be so accurately limited.

I have a number of times excised tubercles or destroyed them with caustic potash, and the wounds healed promptly. The same procedure may be employed in removing circumscribed masses of tubercles along the superciliary ridge or elsewhere. Unfortunately the tubercles may reappear in the skin around the cicatrices, but for a time at least the effect upon the patient's general condition is most salutary. In one case I excised a piece of pigmented skin from the back of an anæsthetic patient. Although the line of incision was carried well beyond the pigmented border, the pigmentation became a year later well marked in the skin surrounding the cicatrix.

The occurrence of gangrene, necrosis of bones, perforating ulcers involving not only the extremities, but threatening important organs, as the nose, throat, and larynx, has necessitated a number of surgical expedients.

Amputations through the thigh, knee, leg, ankle, or arm are most frequently performed for leprous gangrene and ulceration of the extremities.

Perforating Ulcer.—Free incisions down to the bone in perforating ulcers and sinuses leading to dead bone give great relief from pain. In all cases the incision should be sufficient to permit the removal of all necrosed bone to insure healing.

In perforating ulcers of the sole, Beaven Rake recommends that the bistoury be thrust through the foot from the sole, coming out

through the dorsum or between the toes; if the ulcer is near one side, the knife should be brought out laterally, the gaping wound being packed with lint and allowed to granulate.

In deep ulcerations of the lower extremity, which interfere seriously with the patient's comfort and locomotion, the gangrenous flesh should be cut away, any necrosed bone removed, and the parts dressed aseptically. Amputation may be employed in gangrene of the fingers and toes, as it gives a better result than the spontaneous amputation of nature.

When the bone comes away piecemeal, as it often does in these cases, the process is long and painful, and a flail-like condition of the member is apt to ensue.

Of the 830 removals of bone in Beaven Rake's series of cases, 532 were in anæsthetic lepers, 6 in tubercular lepers, and 92 in cases of the mixed type.

In diffuse brawny swellings without suppuration of the lower extremities, long free incisions from the knee to the ankle or from the ankle to the toes are recommended, as they relieve pain and tension from the œdematous infiltration.

Operations on the hands and feet of anæsthetic patients may be performed in many instances without anæsthetics as the parts are devoid of sensation. Patients frequently chop off a useless member without flinching.

Nerve-stretching, for the relief of distressing neuralgia and pain along the course of nerves, and the healing of perforating ulcers in areas supplied by the nerves, has been practised by Beaven Rake, Neve, and others with good results.

Neve, of Kashmir, reports that in 100 cases of leprosy the nerves were stretched 270 times. Great improvement was noted in the tracts supplied by the nerves, except in the face and parts supplied by the cranial nerves. Neve regards "nerve-stretching most valuable as a palliative."

Beaven Rake practised this procedure 113 times on lepers in the Trinidad Asylum. He gives detailed accounts of the results in 100 operations on 60 patients: the sciatic was stretched 26 times, the external popliteal 11 times, the median 14 times, the ulnar at the elbow 18 times and above the wrist 4 times, and the supraorbital once.

The operation was done for ulceration 38 times; for pain 9 times; for anæsthesia 33 times; pain vanished at once, with some improvement, though not complete or permanent; in tubercular cases 18 times; no result. About one-half of the patients were benefited. Rake thought that the chief value of the operation was demonstrated in perforating ulcer, some cases of necrosis and pain associated with

perforating ulcer or peripheral neuritis. He found that the nerves operated on were enlarged in 48 cases.

Beaven Rake's theory of the *rationale* of this operation is that the results are due to changes in the spinal ganglia produced by the stretching. Another theory is that the stretching to which the swollen and congested nerves are subjected empties the blood-vessels and lymphatic spaces of the affected part, and thus relieves the congestion and improves the condition of the patient.

The ocular lesions of leprosy are very common and most distressing. Leloir noted that of 64 lepers at Molde, in Norway, 41 had ophthalmic lesions, 37 in both eyes, while 6 were entirely blind. When there was an invasion of the cornea, Daniellsen and Boeck arrested the progress of the tubercles by cauterizing the conjunctiva or cornea around the tubercles. The tubercles which form on the conjunctiva may be removed from time to time with curved scissors. Kaurin performed keratotomy for the same purpose. Ligation of the vessels supplying the tubercles has been successfully done. The operation sometimes checks the growth of the tubercles temporarily, but it is only palliative. As soon as the collateral circulation becomes established the tubercle again increases. Various delicate operations have been successfully performed with the object of correcting the epiphora and other disagreeable symptoms which result from the paralysis of the orbicular muscle and consequent inability to close the eyelids. For paralytic ectropion Kaurin performed tarsorrhaphy of the inner third of the eyelids, thus raising the lower lid and permitting their closure. Cataract is common in leprosy, and extraction may be successfully performed, oftentimes without an anæsthetic, as the parts are devoid of feeling. Iridectomy has also been employed in cases in which total blindness is threatened.

The lesions of the nose, mouth, and throat, the secretions from which emit a most offensive odor, especially in the ulcerative stage, and are most deleterious to the patient from being constantly swallowed, should be treated with medicated sprays, antiseptic douches, or caustics. For the purpose of destroying leprous lesions of the nasal fossæ and of the buccopharyngeal cavity the thermo- or galvanocautery will be found most available. In the local treatment of leprosy of the upper air and food passages all the resources of the rhinologist and laryngologist should be brought into requisition—cauterizations, irrigations, insufflations of liquids or powders which are employed in the special treatment of affections of these parts. Tracheotomy has been repeatedly performed for dysphagia and stenosis of the larynx, due to invasion of leprous neoplasms. In Nor-

way, Abraham observed one patient who had worn a tube for three years, another for seven years, and another for ten years. In other cases the larynx had become functionally useful and the tubes were discarded.

Hygienic Treatment.

Among the means which experience has shown to influence most favorably the course of leprosy are good hygienic conditions. If the interest of the leper alone were to be consulted, his removal to a country where leprosy is not endemic would be recommended. The most favorable conditions comprise residence in a temperate climate, well-ventilated rooms, freedom from exposure to damp and cold, care of the skin by frequent warm baths, massage, warm woollen clothing, exercise in the open air, and an abundance of nutritious food, fresh meat, vegetables, milk, etc. Baths should be especially insisted upon in the ulcerative period, followed by emollient, soothing ointments, since on account of the suppression of the functions of the cutaneous glands the skin becomes dry, fissured, and covered with the products of the suppurative lesions.

Since traumatisms and injuries are often the starting-points of obstinate and destructive ulcerations, we should carefully guard against all exposure to external causes of irritation and wounds of the integuments. The eyes should be protected from contact of dust and other irritant particles.

The individual capacity of resistance should be strengthened by all measures calculated to build up and maintain the general health at the highest possible standard.

General Conclusions.

The following conclusions may be formulated as embodying the author's views upon treatment:

Leprosy is in the vast majority of cases an incurable disease.

There is no substance known to science which, introduced into the body, is capable of destroying the bacilli without destroying the living cells which contain them.

Furthermore, from the nature of the pathological changes and the position of the bacilli in the deeper tissues, it is evident that no germicidal agent can be brought into direct contact with the pathogenic organisms, and hence all treatment which has for its object the destruction of the bacilli is impossible of application.

The treatment of leprosy has been essentially empirical; whether, as has been claimed, certain remedies act by virtue of their sterilizing

properties upon the living tissues, rendering them unsuitable to the growth and multiplication of the bacilli, cannot be determined.

The special remedies which clinical experience would indicate to be of the most value are chaulmoogra oil, gurjun oil, and certain agents of the Strychnos family; all are, however, more or less disappointing in their results.

All observers agree that in advanced cases, when general dissemination of the bacilli has taken place, curative treatment is absolutely futile. The most favorable conditions are that treatment be instituted early, and that it be prosecuted actively and energetically during a prolonged period.

The serum therapy of leprosy, by the injection of the Carrasquilla serum and other antileprotic serums, has not fulfilled the expectations of its value. In the hands of numerous experimenters its use has been condemned by its clinical results.

The treatment of leprosy by injections of tuberculin has been disappointing in its results. Experiment has shown that the action of tuberculin is positively pernicious in setting free the bacilli in the tissues and determining the development of new foci of the disease.

The more or less rapid development of leprosy depends upon the resistance of the tissues to the inroads of the bacilli. In exceptional but well-authenticated cases, this capacity of resistance is sufficient to dominate and destroy the pathogenic microbes, as shown by the observation of abortive cases in which indubitable signs of the disease definitely disappear and never recur.

This capacity of resistance may be strengthened by change of climate, improved habits of living, and measures calculated to build up and maintain the general health at the highest standard.

Observation shows that the removal of a leper from an infected district to a more favored climate exerts a marked modification upon the course of the disease; there is, for a time at least, an arrest or retrogression of the symptoms. This lull in the manifestations is, as a rule, disappointing in its duration. Of the one hundred and sixty-eight Norwegian lepers who have emigrated to this country, there is no record of a single definite cure.

A dry, moderately cool, mountain atmosphere is most favorable in its influence upon the disease. A hot moist climate, or a damp cold climate are both unfavorable.

A nutritious diet of fresh meat and vegetables, warm clothing, exercise in the open air, and freedom from exposure to damp and cold, are important elements in the hygienic course of treatment.

The care of the skin by frequent hot baths, massage, with inunc-

tions of oils, etc., should receive as much attention as the constitutional treatment.

The surgical treatment of leprous sores, necrosed bones, perforating ulcers, the excision of tubercles, amputation of the members, tracheotomy, various delicate operations about the eye, nerve-stretching for the relief of pain, and the removal of threatening complications are of the most signal benefit.

Finally, we may conclude that while medical science holds out no definite promise of cure to the leper, its resources are sufficient to arrest or retard the progress of his disease, to promote his comfort, and to prolong his life.

PROPHYLAXIS.

In dealing with diseases which are confessedly beyond our therapeutic resources prophylactic measures become magnified in importance. In the case of leprosy the uniform failure of all specific curative treatment which has been thus far instituted gives an added prominence to the value of preventive treatment.

Within recent times the prevention of the spread of leprosy has become a question of live practical interest to our sanitary authorities. The development of new epidemic and endemic centres of the disease in various countries previously exempt, its reawakening into activity in countries where it was supposed to have become extinct, and its undoubted spread in many parts of the world have stimulated a renewed interest in its study, especially of the sanitary measures best adapted for its suppression or control. The principal object of the convocation of the International Congress of Leprologists which convened in Berlin in October, 1897, as set forth in the call, was "to consider the best means for the entire suppression of leprosy." The motive of the call was stated to be the "danger of a new pandemic outbreak of leprosy on the European continent." While a conviction of the imminence of such danger is not shared by the writer, it must be admitted that with the beginning of the twentieth century both Europe and the United States are confronted with conditions which may render leprosy a serious menace to the public health of these countries. Some of these conditions may be briefly referred to.

At the present time the ambition for territorial expansion and the desire for colonial possessions which have seized upon the dominant nations of Europe have extended to this country, and the retention of recent territorial acquisitions seems to have been accepted as a settled policy for the future. The genius of modern civilization appears to be directed in the line of appropriating the territories of the older countries, China, India, Africa, and partitioning them among

the younger and more aggressive nations. It must not be forgotten, however, that, in opening wide the doors of communication and intercourse with these older semi-civilized nations in which plagues and pestilences have been domiciled for centuries, we are also brought closely in contact with the diseases to which they are subject. It is probable that many of our soldiers who form the army of occupation in Cuba, Porto Rico, and the Philippines will bring back leprosy as a souvenir of their sojourn in these islands. The significance of possible danger to the health interests of modern civilized countries from this source has been recognized, and schools for the study of tropical diseases have been established with the view of employing the means and appliances of scientific medicine in their study, and utilizing the resources of modern sanitary science in their prevention and cure.

In addition to the enlarged facilities for rapid communication and intercourse between the peoples of different countries, the opening up of trade and commerce, and the creation of new business and industrial enterprises, the commercial proximity thus established tends to bring infected and non-infected races into closer and more intimate relations. Our extensive maritime relations with other countries in which leprosy is endemic will enable leper subjects to find ready transportation to our shores, and there is every reason to fear that leprosy may eventually come to be one of our current maladies. The only question is whether leprosy can survive the contact of civilization; whether the better stamina of the people, the improved hygiene public and private, and our modern methods of sanitary supervision will be sufficiently strong to cope with the disease.

It is a fact worthy of consideration that the colonies of every European country, with scarcely an exception, are infected with leprosy, and the same may be said of the recent territorial acquisitions of this country. The United States in annexing Hawaii has incorporated a native population tainted with leprosy. In absorbing Porto Rico, and in establishing a protectorate over Cuba, our people have been brought into most intimate commercial and social relations with the leprous inhabitants of these countries. In appropriating the Philippine Islands we have become possessed of one of the most important centres of leprosy in the far East, and which, from its proximity to the "Cradle of Leprosy," in Kwang-Tung and Hong-Kong, must be exposed to continued invasion of fresh increments of infected material in the Chinese coolie lepers. It is probable also that Japan will furnish a contingent of leprous immigrants from among its overcrowded and non-productive population. The danger will probably be not so much from the importation of native leper

immigrants from these colonies, but from the exposure of our own people, who will be attracted by considerations of trade or commerce, to contact with the leper population. The lepers that have recruited European countries in the present century have been almost without exception sailors, soldiers, or official representatives of the administrative departments who have sojourned for a longer or shorter period in the leper colonies. In throwing wide open the portals of communication between our own and leprous countries we are virtually releasing the diseases which had been secluded behind the closed doors of caste and insular prejudice for ages. These facts have a most important bearing upon the prophylaxis of leprosy.

In the study of the prophylaxis of leprosy the teachings of the observation and experience of other countries and other ages should be utilized. First in point of antiquity, as well as of extensive experimentation, may be considered the isolation or segregation of lepers. In appreciating the value of this method and its adaptation to the conditions of the leprosy problem as it presents itself at the present day, we may inquire into its utility as a prophylactic measure applied to diseases in general and the practical results of its application to leprosy in particular.

The separation of the sick from the well as a means of preventing the spread of disease is based upon science and common sense, and has been sanctioned by the results of experience in all ages. So far as any sanitary procedure can be regarded as inspired, the separation of the clean from the unclean may be considered a divinely appointed measure for the prevention of disease. Leprosy enjoys the distinction of having been the first, and for many centuries the only, disease to which this cardinal principle of preventive medicine was applied. Indeed, sanitary science may be said to have had its origin in the measures of isolation and segregation which were instituted in ancient times for the control of leprosy. While the wisdom of this prophylactic measure is under certain conditions unquestionable, the method of its practical application in earlier times cannot be commended.

Under the Mosaic law it was rigorously enforced with the strictness with which punishment is meted out to crime, but with a lack of discrimination and humanity which could be justified only by the semi-civilized conditions of the age. Leprosy was regarded as a mark of divine disfavor, a retribution for sin, and human approval of divine judgment was shown by cruelty, oppression, and persecution. It is worthy of note that this traditional conception of the moral etiology of leprosy still survives in certain Oriental countries. In China, India, and Japan at the present day leprosy is accepted as a punishment for sins committed by the individual or by his ances-

tors, and lepers visit shrines and holy places in expatiation of these fancied sins. At a later period in Jewish history the Divine Physician seems to have shown a special tenderness and consideration for lepers, which markedly contrasts with the sentiment of hostility and ostracism that characterized the spirit of the old Hebraic law.

For many centuries the severe and cruel measures formulated in the Levitical code for the repression of leprosy were preserved and perpetuated. In the Middle Ages, when Europe was overrun with the plague of leprosy, the regulations for its repression exhibited the same spirit of harshness and persecution as animated the Jewish lawgivers. The leper was separated from his family and friends, his marriage was annulled, his civil rights were abrogated, and he was pronounced legally dead, and incarcerated in a lazaretto until death should release him. If we compare these prophylactic measures with those of barbarous and uncivilized countries, we shall find that the principal difference was in the greater sanctity in which human life was held by the Jews and Christians. The aboriginal methods were much more summary, but perhaps more merciful, in the swift ending of the patient's suffering. In Africa, Sumatra, the Fiji Islands, and many other uncivilized countries, the aborigines were in the habit of privately killing lepers and burning their bodies.

If we contrast the ancient methods of dealing with leprosy with those practised in modern times, it is evident that the tendency is towards a more intelligent and humane treatment of lepers, although the traditional spirit of intolerance, ostracism, and persecution still survives in many countries.

The chaotic confusion of skin diseases has been cleared up, and, thanks to our greater precision of diagnosis, it is exceptional for other forms of disease to be confounded with leprosy. Again, under the sanitary policy of many enlightened governments proscriptive measures are now enforced not only with a more intelligent discrimination, but also with more humanity.

So far as we know, leprosy was the only disease to which segregation was applied in earlier times. In modern times the principle has been extended in its application to a large group of diseases which come within the category of contagious or infections diseases. At the same time there are certain other diseases of a recognized contagious nature which do not come within the provisions of compulsory notification and isolation; for example, varicella is not isolated, although equally contagious with smallpox, because it is a mild disease and not a cause of death.

The isolation of venereal diseases is not regarded as feasible or practicable, largely because they are private or secret, and the risk to

others of contagion is chiefly due to the voluntary exposure of the healthy to contact with the diseased. Syphilis is perhaps an exception, although the cases of syphilis insontium are comparatively few. In regard to these diseases, it is admitted that they may be severe in their effects, both immediate and remote; they entail suffering and may endanger life; they have an important socio-economic relation to the public health so far as their incapacitating effect upon wage-earners, army and navy invalidism, etc., is concerned, and also in their undoubted influence as a factor in the depopulation of countries. The individual liberty of these diseases is protected by their nature, their secrecy, and furthermore, perhaps, by the failure of all measures hitherto proposed for their correction.

Tuberculosis, the modern Samson among diseases, which slays its tens of thousands, while smallpox, measles, scarlatina, etc., slay their hundreds or thousands, is recognized as a contagious and infectious disease, yet modern sanitary science has not placed it under the ban of notifiable diseases. This is because of its widespread prevalence, the impossibility of isolating and supporting the great army of consumptives, and the fear of infringing upon the rights of the individual; again, because of its chronicity. Isolation contemplates brevity, and finds its proper application in diseases which are of short duration, and render the patient temporarily unable to care for himself. But a consumptive may not be incapacitated for business; he may have years of usefulness and life before him. The disease does not place him *hors du combat* in the battle of life. Indeed, he may hope for a comparative or even complete cure. Sanitary science cannot attack or apprehend him in these strongholds. The result is that the sanitary supervision of tuberculosis is restricted to the disinfection or destruction so far as practicable of the sputa containing the disease germs, the education of the patient as to the risk he carries to others and the best means to avoid those risks, and the establishment of sanatoria in favored regions for the cure or amelioration of the disease.

In leprosy we have a disease which presents many analogies with tuberculosis. As has already been said, there is no infectious disease so mild in its initial manifestations as leprosy. There is no disease of a necessarily fatal character which grants its victim so long a lease of life; even after characteristic evidences of the disease are manifest the patient may live in comparative health for many years, with faculties unimpaired, and the capacity for usefulness and work practically undiminished. This is especially true of anæsthetic cases. It may be questioned whether it is just, humane, or necessary for the protection of society in countries where leprosy does not seriously menace

the public health to incarcerate such a person in a lazaretto until death releases him.

It will be seen that mere isolation of the sick by no means represents the highest wisdom of sanitary science or the perfection of sanitary methods. The diseases to which it is applicable are to be differentiated, not only from the point of view of their gravity, but from that of their prevalence and their tendency to propagate themselves, and it is to be adapted to the peculiarities of each particular disease. The science of modern preventive medicine takes into account, not only the nature and contagiousness of a disease, but also the degree of its contagious activity and the conditions under which this contagion operates. The behavior of the disease as modified by these conditions, and its epidemic, endemic, or sporadic character are to be considered in determining the character of the sanitary measures to be employed for its control. Each disease must be studied in relation to its environment, the character of the soil, and the conditions which favor or lessen its tendency to spread. We do not apply, nor do we deem necessary, the same sanitary regulations for yellow fever in New York or the City of Mexico as for the same disease in Havana or Vera Cruz, because the conditions which favor its spread exist in the two latter cities, but not in the former.

Leprosy does not comport itself as a contagious disease under all conditions of environment. Its contagious mode is a law unto itself. It shows the most remarkable variations in its virulence and in its development and decline. In some countries its contagious virulence is manifest with all the characteristics of a violent epidemic. In other countries its contagiousness is mild, scarcely manifest. It is an error to suppose that in all countries where leprosy is introduced it will necessarily spread, or that every leper will communicate his disease to those with whom he comes in contact. It is equally erroneous to conclude that we possess in segregation or isolation an infallible or sure cure for the prevention of leprosy, or that these measures employed in the most active, energetic, and vigorous manner will infallibly cut short its epidemic violence. It may be claimed that segregation constitutes the best means known to sanitary science for the prevention of leprosy, but the indications for its employment are to be differentiated and adapted according to the manifestations of its contagious power in different countries and the degree of their leprous contamination.

We may now inquire what has been the practical result of segregation in certain countries where it has been applied. The successful results of segregation are claimed to have been most brilliantly illustrated in the extinction of the leprosy epidemic of the Middle

Ages, and in more recent times in the marked decline of the Norway epidemic. It may be observed that a great many intelligent and judicious students of the history of leprosy insist that the cause of the progressive diminution of the disease in the fourteenth and fifteenth centuries and of its practical disappearance from Europe in the sixteenth and seventeenth centuries was not due to the admittedly imperfect system of segregation then employed, but should rather be ascribed to the improvement in the material hygienic and social conditions of the people; to the better food, better habitations, and the increase in material prosperity. In the Middle Ages strict segregation, if we are to trust historical evidence, was never carried out.

Newman, in his prize essay on "The History of the Decline and Final Extinction of Leprosy as an Endemic Disease in the British Islands" (New Sydenham Society, 1895), believes that probably the famine (1315) and black death (1349) materially assisted in the extermination of lepers in the fourteenth century. He believes that the decline and final extinction of endemic leprosy was due not to segregation, but to the general and extensive social improvement in the life of the people and to a complete change in the poor and insufficient diet, the agricultural advancement, improved sanitary and land drainage, etc.

Jonathan Hutchinson is also inclined to the belief that segregation exerted little influence in the decline of the mediæval epidemic, but that it took place by slow degrees *pari passu* with the advance of agriculture and in social comfort.

As regards the decrease of leprosy in Norway, it may be said that no effective system of isolation or segregation worthy the name has ever been carried out in that country. Before 1885 the lepers, except a limited number who were unable to provide for themselves, did not enter the hospitals. Entrance into the leprosy hospitals was voluntary, not compulsory, and lepers were free to come and go. Moreover, leprosy had already begun to decrease before 1885, at which date the leprosy law was enacted which made entrance into the hospital compulsory for paupers who could not provide for their own wants. "The leper, if he will live at home, must have his own room, at least his own bed, his clothes must be washed separately, he must have his own eating apparatus—spoon, knife, fork, etc. If he cannot or will not comply with this regime, he is obliged to enter an asylum."

It is generally conceded that the leprosy laws of Hawaii are more complete and rigorous and are enforced with more strictness and impartiality than in any country in the world. Segregation has been practised for over a third of a century in these islands with a vigor

and severity which would not be possible among a people who were jealous of their personal rights or individual liberty. What has been the result of this thirty-five years' crusade against leprosy? Is it on the increase, or is it in process of extermination? Taking the records of the leper settlement as a basis of comparison, there would seem to be no favorable sign of its extinction. In the first twenty years of its establishment 3,076 lepers, in the next ten years 2,049 were consigned to the leper settlement. This large relative increase of admissions, it is claimed, may be due not to an actual increase in the number of lepers in the islands, but to a more active and vigorous method of segregation within the last ten years. In the first-mentioned period the number of lepers at the settlement ranged from two hundred to eight hundred. In recent years the number has varied from one thousand to twelve hundred, and the annual consignment of lepers shows little diminution in number from year to year.

Segregation must always be a defective measure from the very nature of the disease, simply because all cases of leprosy cannot be brought within the sphere of its operation. No official dragnet can ever be constructed which will gather up all the lepers in any country. The little fishes, the latent, incipient lepers will escape. Segregation, although incomplete, undoubtedly tends to limit the spread of the disease by removing or rendering innocuous just so many sources of contagion.

Experience teaches us that harsh measures of isolation and segregation always defeat the object in view because their chief result is the concealment of cases. Unless human nature changes, the more rigorous and severe the measures adopted the greater will be the incentive to evade and escape their operation, no matter how beneficent their purpose. In South Africa the recent leprosy commission came to the conclusion that the attempt to send all lepers to Robben Island only led to many lepers being hidden throughout the country. In the Berlin Leprosy Congress Alvarez of Honolulu declared his "opposition to the adoption of rigorous or cruel measures against leprosy in Hawaii, not only because they led to the concealment of cases, and thus defeated the object for which they are designed, but because we ought to adhere to principles of humanity and not treat the lepers as if they were criminals."

Similar results from the operation of strict segregation laws have been observed in all countries where an attempt has been made to enforce them.

While allowing segregation to be the most effective measure known to sanitary science for the prevention of leprosy, its application is not universally practicable. In India segregation is not practicable be-

cause of the number of lepers. Any government would stand appalled and helpless before the task of segregating and supporting more than one hundred thousand individuals. The same consideration applies to leprosy in China and Japan.

Again, the social and political conditions in different countries must be considered in applying measures which infringe upon personal liberty. Serious difficulty was met with in India recently in endeavoring to induce the people to adopt simple sanitary precautions against the plague, an acute and fatal disease. One may appreciate the difficulties to be surmounted in instituting harsh measures against a disease which has existed in permanence among them from time immemorial.

It must be remembered that in old countries where leprosy has existed for centuries there are deep-rooted customs which seem almost as sacred as religious observances and which have all the force of unwritten laws; these customs cannot be eradicated without opposition or open revolt. It is not possible for any government by compulsory laws to compel such people to have recourse to national establishments for isolation and treatment.

It was with a full knowledge of these facts that the Berlin Leprosy Congress unanimously adopted the following resolutions as embracing the views of the congress upon the best means to be employed for the control and suppression of leprosy.

First, in such countries where leprosy is endemic, and in all countries where leprosy forms foci or has a great extension, isolation is the best means of preventing the spread of the disease.

Second, the system of obligatory notification and surveillance and isolation, as practised in Norway, should be recommended to all nations with local self-government and a sufficient number of physicians.

Third, it should be left to the administrative authorities after consultation with the medical authorities to take such measures as are applicable to the special social conditions in each country.

These recommendations seem eminently wise and judicious and coincide for the most part with the views expressed by the writer several years ago. As regards "obligatory notification," it may be said that the wisdom of a measure which renders it obligatory on the part of physicians to report to the sanitary authorities every case of leprosy coming under their observation is questionable in countries when leprosy does not prevail to an alarming extent. In countries where segregation is compulsory, notification is, of course, necessary to the effectiveness and success of the scheme. In this country it might serve to locate a few cases of leprosy unknown to the

authorities, but unless they are empowered to isolate such cases they could exercise over them only a sort of sanitary surveillance of doubtful utility, and which, if oppressive, would result in the migration of the leper to another locality. The action of the Philadelphia board of health a few years ago in fining a physician for not reporting two cases of leprosy under his care was generally condemned by the medical profession.

Another aspect of the question is worthy of consideration. In countries where leprosy is not endemic few physicians have ever seen a case. They are not familiar with the clinical features of the disease and are therefore not competent to make a diagnosis. The verdict of leprosy carries with it a grave responsibility, and should never be pronounced, or at least accepted, as final unless confirmed by a special board of competent experts. The consequences to the individual are of such a serious character that the same care and intelligent skill should be exercised as contemplated in the law which provides for a commission of lunacy to inquire into the mental soundness of an individual.

One prophylactic measure which meets with universal acceptance is the endeavor to confine leprosy in countries where it already exists and prevent its extension in countries exempt or but slightly infected, by the exclusion of all leprous immigrants. As will be seen in another section of this article, quarantine laws prohibiting the introduction of leprous immigrants have been enacted by various governments, and their strict enforcement guaranteed by a heavy penalty of fine or imprisonment for violation of their provisions, but from the very nature of the disease this measure is only partially effective.

As I wrote several years ago, "no system of quarantine has ever been devised which will effectively prevent the importation of a disease so insidious in its development or so little manifest on ordinary inspection as leprosy."

A thorough examination for signs of leprosy would necessitate the stripping of the entire body, so that every portion of the cutaneous surface might be subjected to inspection—a procedure which for many reasons is entirely impracticable.

Hansen says: "I have been given the names of many lepers in America whom we did not know to be lepers when they left Norway. A majority of them have got distinct eruptions after their arrival in America. Even after the most scrupulous examination of these people at the time of their departure from Norway we could not have been able to diagnosticate their disease, and any prohibition of the immigration of lepers will be for the same reason useless." According to Bracken, "it would be far more probable to say that

twenty-five of the fifty-one lepers had the disease before leaving Europe."

That we are constantly importing leprosy is a recognized fact. Quarantine protection could be made more effective by international coöperation between governments in which not only the leper immigrant, but all immigrants coming from leprous families, should be examined before they embark, and even if they show no signs of the disease, they should be kept under surveillance for several years after they arrive in the new country in order to watch for developments. The good effect of such a system is shown in the working of the international laws regulating the importation of Japanese contract laborers into Hawaii. The Japanese laborers are examined before leaving their own country and also upon their arrival in Hawaii. During the period in which these laws have been in operation among the twenty-eight thousand Japanese laborers who have been brought to Hawaii only six cases of leprosy developed, and these were returned to Japan.

At the present day there is a wide difference in opinion among leprologists as well as sanitary authorities respecting the value, or rather the necessity, of employing compulsory segregation for the suppression of leprosy in this country and Europe. Some contend that such radical measures constitute the only effective means at our command for the control of the disease, and they formulate the proposition that every leper, whenever and wherever found, should be at once isolated from all contact with healthy individuals and that this compulsory isolation should be enforced by government edict. It may be said that a sanitary measure for the prevention of every disease is like a panacea for the cure of all diseases: "what is good for all is good for nothing." There is no doubt that an unreasoning enthusiasm often obscures the judgment and blinds the critical faculty, so that one cannot intelligently decide as to the real value or efficiency of a proposed measure. Just as in the curative treatment of disease the indications vary according to the nature and course of the individual disease, so sanitary and prophylactic measures must be adapted to the character and the contagious mode of the particular disease. They must be specialized or individualized. Under certain conditions an expectant treatment, meeting the indications as they arise, is all that is necessary. Under other conditions the treatment must be energized. In other words, it must be symptomatic and adapted to the peculiarities of the individual disease.

It is important, first of all, to know the characteristics and course of leprosy in a community or country in order to appreciate and measure the prophylactic means which should be directed to its control. In

dealing with a disease so irregular and so variable in its contagious activity, which seems to differ widely in different countries and in different epochs under conditions which we can neither control nor comprehend, it is evident that we cannot formulate regulations which are universally applicable to all countries irrespective of the behavior of the disease, its tendency to spread, and the degree of their leprous contamination.

In a country where leprosy is epidemic, as in the Sandwich Islands, where there is great promiscuity in the habits of eating and drinking and the mode of life is essentially communistic, where the natives are too ignorant or indifferent to observe those precautions which science has indicated as necessary to avoid contagion, and above all where the disease manifests itself with intense virulence, strict segregation is a necessary protective measure. But in this country, where the habits of life are different, where persons are non-communistic in the matters of eating and drinking and sleeping, and where observation has shown that the disease has a tendency to die out from natural causes rather than to propagate itself, such harsh measures would be cruel and inhuman, as they are unnecessary. It would be absurd to apply the same repressive measures for the control of leprosy in England and France as in their colonies in South Africa and New Caledonia, where the natives are dirty and promiscuous in their habits, communistic in their modes of living, and who do not fear, but ignorantly invite contagion.

From the above it is not to be inferred that the writer is an opponent of segregation; on the contrary, he believes that segregation is the most effective measure that can be employed to limit the spread of leprosy, and in some countries it is a necessary measure; but he does not believe that it can ever result in the entire suppression of leprosy, largely because of the nature of the disease and the impossibility of making it thorough and complete. Upon this point may be quoted the writer's views, expressed several years ago: "There can be no doubt that if every leper on the face of the globe were removed from all contact or communication with the healthy the disease would become extinct with the death of the present leper population. But isolation or segregation of lepers in special communities or hospitals, in order to be effective, must be thorough and complete. In countries where the compulsory segregation of lepers has been enacted by legislative authority its thorough enforcement has been found to be impracticable. Even in the Hawaiian Islands, where the energies of the Government have for years been directed to this end with all possible vigor, it has failed to accomplish the object. Doubtless these measures have checked the disease, but the latter shows no signs of extinction.

"The causes of this failure are probably due largely to the insidious character of the disease. In every country where leprosy is endemic a large number of persons are infected months and years before it is known to themselves or to others. Now unless leprosy is devoid of contagious activity in the earlier stages segregation of this class is absolutely essential to the effectiveness of the scheme. If such cases are contagious, they are most dangerous since their intercourse with family and friends is not restricted by the wholesome disgust which the disease in the later stage always inspires. Again, many lepers present in their face no visible sign of the disease, or they manage to conceal all convicting evidence for many years after it has developed. Such persons must be active spreaders of the contagion.

"In this country, the compulsory segregation of lepers in lazarettos, as has been recommended by some of our health authorities, can scarcely be considered a necessary protective measure. Wherever leprosy has been introduced, except in the moist, warm climate of our Southern seaboard (Louisiana and Key West), it does not show an alarming tendency to spread and develop new foci of infection. Professional as well as public sentiment is opposed to the adoption of harsh coercive measures to crush out an evil which does not seriously menace the public health, but rather tends to die out from natural causes."

The endemic outbreak of leprosy in Louisiana, where the disease had been quiescent and apparently extinct for a century or more, shows conclusively that no measures for the control of leprosy can be considered absolute or permanent. They must be modified and adapted to changing conditions as they arise. Twenty-five years ago the necessity of taking active measures for the suppression of leprosy in that State would not have been considered urgent; but the recent statistics of leprosy in Louisiana show that the disease is spreading and rapidly assuming alarming proportions. This is only another illustration of the variability in the contagious activity of leprosy, which manifests marked modifications in its virulence accordingly as the conditions which influence its development and spread are present or absent. In Louisiana an attempt has been made to prevent a farther spread of the disease by the establishment of a leper asylum, and while the advantages afforded by this institution have been accepted by a limited proportion of the leper population, the larger number of lepers is still at large.

In this country there is no possible protection against the spread of leprosy by the enactment of laws for the segregation of lepers by the different States. Segregation by single States is not practicable. The result would be to drive lepers from States enforcing such practice to States where segregation was not practised.

Leprosy in the United States should be under the control of the national Government. If in the opinion of our sanitary authorities leprosy prevails in any State or section of this country to such an extent as to prove a serious menace to the public health and demands the segregation of the few for the protection of the many, homes or asylums with suitable hygienic surroundings should be provided for the care and maintenance of lepers by the national Government. Such asylums should be made comfortable and attractive and arranged with special adaptation to the requirements and peculiar needs of their inmates. In view of the chronicity of the disease, lepers should not be condemned to confinement and inactivity, but should be provided with interests, means of employment, and recreation. As a large proportion of lepers are able to engage in some kind of industry, such institutions might be made partly or wholly self-sustaining from the proceeds of their industries. They might be conducted as colonies, and provision should be made for giving occupation to those able to work.

Many lepers would doubtless avail themselves of the advantages of such an institution. There comes a time in the history of almost every leper when he recognizes himself as an object of disgust and pity to his family and friends, when he would be glad of an asylum in which to end his miserable existence. Again, there are many lepers who would gladly go to such a refuge as soon as the nature of their disease is evident, for fear of spreading the contagion to their families or friends.

An intelligent discrimination should be exercised in selecting cases suitable for segregation.

While we know nothing definitely of the modes of infection or the conditions under which it takes place, we recognize Hansen's bacillus as the active efficient cause of leprosy. Its degree of contagiousness will depend upon the type of the disease and its stage of development. In the pure type of anæsthetic leprosy the bacilli remain for many years localized in the nerve tissues and are not found in the cutaneous lesions. Such patients are probably exempt from all possibility of danger to others until at an advanced stage, when the tissues break down and liberate the bacilli. In the writer's opinion such cases bear much the same relation to the tubercular form, from the point of view of contagion, as fibroid phthisis does to acute or chronic pulmonary tuberculosis.

Lepers in good circumstances, able to provide themselves with separate homes, and whose intercourse with the healthy could be restricted under sanitary surveillance, should not be subject to segregation. Observation shows that if a leper lives by himself, with sep-

arate room, bed, board, etc., and does not come in intimate contact with others, he is practically innocuous so far as contagion is concerned. In cases in which such conditions cannot be complied with the leper should be placed in a hospital or asylum specially provided for this class of patients.

Wherever he may be placed, the leper himself, as well as his habitation, should be kept scrupulously clean. In view of the fact that contamination probably takes place chiefly from the nasal or buccal excretions, these should be disinfected or destroyed with the same care that would be exercised in cases of tuberculosis. In addition strict antiseptic and occlusive dressings should be applied to all open sores or ulcerations. The garments of the leper should be separately washed, and his clothes, linen, and ordinary objects of use should be regularly disinfected from time to time.

Finally, if lepers are segregated they should receive expert medical care. They should be treated energetically by all known means, external or internal, sanctioned by experience. There is no doubt that the lamentable failure of our therapeutic resources is due largely to the conditions under which they have been applied. The dominant conviction forced upon lepers when placed in a lazaretto is that they are shut up to die, and the utter hopelessness thus engendered renders all treatment a failure. Says a well-known writer: "When a man affected with leprosy is taken from his home and friends, pronounced unclean, immured in a lazaretto with many loathsome fellow-sufferers, and given to understand, as is usually the case, that death is the only portal of escape open to him, the impression upon his mind is such as to counteract the effect of all remedies, and under such circumstances nothing short of a miracle could be expected to effect a cure of leprosy."

There is no doubt that if sanatoriums or colonies were instituted for the reception of lepers, as in the case of tuberculosis, and provided with suitable means of treatment in the earliest stages, many of the cases might be aborted or the further progress of the disease arrested. In view of the incompleteness of our knowledge of leprosy and the necessity for the further study of the life history of the bacillus and the conditions under which it is communicated, a laboratory under the care of an expert physician should be established in connection with every such asylum, for the study of the disease with the aid of modern technique and of the various instruments of precision.

HISTORY.

Leprosy occupies a peculiar position among diseases affecting the human race. It is the most ancient, the most exclusively human, and in the popular conception the most dreaded of all diseases. It is a universal malady, affecting all races and occurring in all climates and under all conditions of life. Although no race is immune, racial peculiarities, climate, and the hygienic habits of civilization undoubtedly modify its spread.

Unlike the plagues and pestilences which formerly swept away entire populations and devastated countries and then disappeared forever, leprosy has at certain periods of the world's history raged as a veritable epidemic and then subsided and apparently disappeared, but has never become extinct. It has preserved its individuality through all the vicissitudes of time. It still survives and maintains its supremacy as the patriarch of diseases.

The origin of leprosy is lost in the night of time. There are certain special circumstances which have made the study of the early history of leprosy one of peculiar difficulty. In endeavoring to trace authentic records of leprosy in the earlier writings, we are confronted with difficulties which arise from the lack of medical knowledge among primeval peoples, their consequent defective description of disease, and their inability to distinguish the morbid phenomena peculiar to different diseases. It could hardly be expected in the undeveloped state of medical science that leprosy or any other disease would be described with that accuracy and minuteness of detail which characterizes the description of disease of the present day. We should expect that only one or more prominent symptoms of the disease which particularly impressed the observer would be mentioned.

Another difficulty arises from the doubt as to the exact meaning to be given the terms employed by ancient writers in designating diseases, and whether the words in different languages which have been translated as leprosy actually referred to the same or to different diseases. In the evolutionary changes to which all languages are subject the primary signification of certain terms is involved in obscurity, and there has always been much diversity of opinion as to the identity of the Hebrew "tsaraath," the Greek "leuké," the Arabian "baras" with modern leprosy, but, irrespective of all these elements of confusion, the fact remains that from the earliest attempts to record the phenomena of disease there may be traced, through the succession of centuries, in the Greek, Arabian, and Roman writings, an unbroken reference to a particular disease, which stands prominently

forth among other diseases, and which powerfully impressed the popular imagination by its severity, its hideous deformity, and its incurability, and which we recognize as leprosy. It is equally certain that many milder forms of disease, which present one or more symptoms in common with this more formidable disease, were included in the category of leprosy. This diagnostic error has been perpetuated through mediæval times and is still committed at the present day.

In the Middle Ages the diagnosis of leprosy was still in a state of chaotic confusion, and in the leproseries were found numerous examples of almost every form of cutaneous disease. Even in countries where leprosy is now endemic the result of the examination of supposed cases of the disease by presumably skilled and competent physicians shows patients in whom the symptoms are suspicious but by no means conclusive.

Although leprosy has existed in all periods of the world's history and afforded abundant opportunities for its observation and study, it is the reproach of medical science that, in some respects, it is to-day the most mysterious and obscure of all diseases, especially in its modes of communication, its variable virulence, and its faculty of remaining latent for a long period and then reawakening into activity.

In explanation of this lack of definite knowledge of the disease it may be said that for several centuries leprosy had practically disappeared from Europe and other civilized countries where medical science was most cultivated and where the capacity of intelligently studying and classifying diseases was most trained and developed. During the seventeenth, eighteenth, and the first half of the nineteenth centuries leprosy had for the medical profession only a historical interest. When an important leprous centre was discovered in Norway about fifty years ago, it was a revelation and a surprise, and leprosy became invested with all the interest of a resurrected disease.

Prior to the appearance of the magisterial work of Daniellsen and Boeck on leprosy, in 1848, the communications in regard to the disease were of a vague and incomplete character, possessing little scientific value and not generally accessible. It may be said that the first opportunity of studying the disease by the methods of modern science was afforded by the Norwegian epidemic, which has been termed the "academy of instruction," in leprosy. The epidemic gave a new interest to the study of the disease by scientific men. Its survival or reappearance in many civilized countries from which it was thought to have definitely disappeared and its undoubted spread in many countries previously exempt have awakened a general interest on the part of the medical profession and stimulated the study of the sanitary measures best adapted to its suppression and control.

Leprosy in Various Countries.

Among the Jews.

Leprosy has the distinction of being more frequently spoken of in the Sacred Scriptures than any other disease. From the frequency with which it is mentioned and the prominence given to the measures instituted by the great Hebrew lawgiver for its repression, it is evident that leprosy overshadowed in importance all other diseases of that period. From the Mosaic writings, the Talmud, and other historical records we have evidence that leprosy was present during the entire period of the early history of the Jews, and that the sanitary regulations prescribed in Leviticus were framed chiefly for the control and suppression of this formidable disease.

It is generally accepted that the Israelites contracted leprosy during their sojourn in Egypt, where it had existed from time immemorial, and that they carried the disease with them during their exodus from Egypt, and that it has existed among them from that time to the present day. At the time of Christ leprosy must have been common in Judea and Palestine, from the frequency with which lepers are mentioned. All evidence points to it being a commonly recognized, if not a prevalent, disease.

The Mosaic account of leprosy forms no exception to the characterization previously made of the description of the disease by other ancient writers, viz., that it is exceedingly vague and indistinct and that it was confounded with many skin diseases of a non-contagious character. It must be remembered, however, that the medical knowledge existing among the Jews at that period was not in advance of that of other nations of the same grade of civilization. We should no more expect that the Mosaic description of leprosy should conform to the clinical description of the modern dermatological writer than that the geological and astronomical teachings of the Bible would be accepted as correct by our modern scientists.

This confusion of dissimilar diseases under the same name and the inability to distinguish between leprosy and affections of the skin are so evident that they have led to a serious doubt on the part of many authorities as to whether the leprosy of the Bible can be identified as the same disease that we now recognize under that name. It is certain that the clinical features and course and especially the rapid evolution of the diseases which were classed as leprosy in the Hebraic records are entirely different from the evolutionary mode of leprosy as we recognize it at the present time.

Thus, for example, the Levitical code provided that successive examinations of the suspected patient should be made at intervals of seven days, thus enabling the priest to note the progress of the disease. Leprosy is so exceedingly slow in its evolution that a fortnight would show absolutely no change in the character of the skin lesions. The thirteenth chapter of Leviticus, in which is given a description of the disease and the signs by which the priests recognized leprosy and differentiated it from other diseases which were not leprous and not contagious, has been analyzed at great length and in detail by many writers on the history of leprosy. Much ingenuity has been displayed in translating or interpreting the terms used by Moses to conform to our modern conception of the clinical features and behavior of leprosy.

Kaposi asserts that the leprosy of the Bible is not leprosy at all, but merely pigment changes which we recognize to-day as vitiligo.

Dr. J. F. Schamberg has recently made a critical study of the nature of the leprosy of the Bible with a view of determining whether it is identical with modern leprosy. He concludes, first, that the Biblical *tsaraath* comprises a number of diseases, chief among which were vitiligo and psoriasis; second, that there is no evidence in the Biblical description to warrant the belief that leprosy existed among the Jews at that period; and third, that the segregation of lepers had its origin in the Biblical example of separating those afflicted with *tsaraath*.

It is generally conceded that both vitiligo and psoriasis were classed in the Levitical code with leprosy. For example, in verses 12 and 13: "And if leprosy shall break out abroad in the skin, and the leprosy covereth all the skin of him that hath the plague from his head even to his feet, then the priest shall consider, and behold if the leprosy hath covered all his flesh he shall pronounce him clean that hath the plague. It hath all turned white and he is clean." This description evidently does not refer to leprosy, but probably to vitiligo. In the opinion of Erasmus Wilson it refers to psoriasis. Again in verses 7 and 8, "but if the scab increase in size and spread after he hath been seen of the priest for his cleansing, he shall be seen of the priest again, and if the priest see that the scab still spreadeth in the skin, then the priest shall pronounce him unclean. It is leprosy." The disease referred to in the above version, according to Dr. Schamberg, is psoriasis, while other commentators regard it as a form of leprosy.

It is not possible for lack of space to enter into an analysis of the arguments used *pro* and *con* as to the identity of the leprosy of the Bible with modern leprosy. While it is certain that nothing corre-

sponding to the objective features of tubercular leprosy can be found in the Mosaic descriptions, there is a general consensus of opinion among authorities that the leprosy of the Bible is nerve leprosy, such as is met with in India and in Palestine at the present day.

Many commentators believe that the affection of Job was tubercular leprosy. Certainly the description of the disease with which Job was afflicted presented striking resemblances to this form of the disease. The fact that Job, Naaman, and others mentioned as being stricken with leprosy were restored to health when suffering from a disease recognized as incurable does not necessarily militate against this view. In the Old-Testament Scriptures both good and evil were attributed to divine agency, and it is not surprising that leprosy was regarded as a manifestation of divine life and punishment for sin, and the cure in any case was regarded as miraculous and the work of divine intervention.

Egypt.

Egypt has been termed the cradle of leprosy. "There is a disease called elephantiasis, which has its rise on the River Nile" (Lucretius). Pliny the Elder, Galen, and other ancient writers refer to Egypt as the home of the disease. There is abundant evidence that it has existed in Egypt from a period of remote antiquity. Archæologists have discovered in papyri found in the tombs of the Pharaohs descriptions which relate to leprosy. In the Medical Papyrus of Berlin there are frequent references to a dangerous and severe disease, "uchetu," which, according to Professor Macalister, of Cambridge, there is sufficient evidence to identify as leprosy. "If so, it seems to have been very common, for both in this work and in the Papyrus Ebers there are many prescriptions for it. The Papyrus Ebers was transcribed in the fifteenth century before Christ, so that if uchetu be the same as the Coptic ouseht which is used in the Pentateuch for leprosy it would be evident that the disease prevailed then."

"The Berlin Papyrus found in the necropolis at Memphis contains many prescriptions for the cure of malignant leprosy, as well as many other kinds of illness and fractures. It was discovered in a writing-case of very ancient origin underneath the feet of the divine Anubis in the town of Sokhem (the Letopolis of the Greeks and Romans) at the time when the deceased Sapti was king (4166 B.C.)" (Thin).

Experts in the Assyrian and Babylonian hieroglyphics state that stones discovered in the ruins of Babylon present inscriptions which relate to leprosy, and they carry imprecations against any one who will dare to touch or displace them.

India.

It is stated that leprosy has existed in India for at least three thousand years. In the earlier times it was called "kushta." Many centuries before Christ, the exact date unknown, Atreya refers to seven varieties of kushta. There can be no doubt that leprosy was common in India six hundred years before Christ (Susruta). Some writers believe that it had its source in China and spread eastward; others believe that it came from India, and others again from Egypt.

China.

There are references in the earlier Chinese writings to a disease which is thought to be leprosy, and there would seem to be no doubt that the disease existed in China long before the Christian era. According to Thin, a writer of the earlier Han dynasty, two thousand years ago, describes a disease which may refer either to leprosy or syphilis. Dr. Monroe suggests that leprosy may have been introduced into China from India, although he infers from the absence of distinct evidence to the contrary in early Chinese writings that the disease was less common in ancient times in China than it is now.

Greece.

It is not known at what precise date leprosy was introduced from Asia into Greece. Hippocrates writes of leprosy, but it is evident that he was acquainted with the disease only from descriptions. He states that the *leukai*, "white diseases," spring from the most deadly diseases, such as what is called the Phœnician disease, and this Phœnician disease has been understood by those who accept that reading to mean leprosy (Thin).

Aristotle, who wrote three hundred and forty-five years before Christ, refers to the Phœnician disease as common in Phœnicia and other Oriental parts, and calls it satyria, in which the countenance seems to resemble that of an animal or a satyr. He compares the term satyria with elephantiasis, a term used by Greek writers for true leprosy. From his description he must have referred to tubercular leprosy. Herodotus, writing four hundred and forty-six years before Christ, was the first to use the word *elephas* for the animal, and he only refers to it as existing in Ethiopia among other wild beasts.

It is probable that at that period leprosy found its way to the coast of Asia Minor near Greece, probably to the latter. It is certain that it was quite common in Greece in the last two centuries before Christ.

Aretæus, who wrote eighty-one years after Christ, and also in the second century, says that elephantiasis is called satyriasis on account of the supposed libidinous tendencies of the patients, while Galen states that the word has been used on account of the resemblance of the leper's face to that of a satyr.

It was called leontiasis by Archigenes, who wrote in 97, and leontia by Aretæus, on account of the supposed resemblance to the leonine face produced by the thickened folds of skin on the forehead.

Aretæus, in the first century of our era, gave a clear and correct description of the clinical features of leprosy. Thin, from whose work the following translation of Aretæus is taken, says in comparing the description of Aretæus with the vague and imperfect allusions in Hebrew, Sanskrit, and Egyptian literature: "We appreciate the enormous intellectual advances which have been made by the genius of the Greek race."

"Formerly this affection was called leontiasis, on account of the resemblance between the disease and the lion, produced by the appearance of the raised part of the forehead, which I shall mention later on; satyriasis, on account of the redness of the cheeks, as well as of the insurmountable and shameless inclination; Herculean, because there is no disease which is graver and more violent. Its power is indeed formidable, for of all diseases it is the one which possesses the most energy.

"Like the elephant, it is terrible and hideous from many points of view. It is irresistible, inasmuch as from the beginning it carries in itself the cause of death; that is to say, a chilling of the congenital heat or a glacial cold like that of a rigorous winter, in which water is transformed into snow or ice—altogether a horrible cause of sickness and death indeed.

"At the beginning the disease is not characterized by any distinctive sign, the patient not being affected by any unusual symptom. It does not show itself at first on the surface of the body, so that it cannot be observed and remedied at the outset, but is concealed in the bowels as in a subterranean abyss, and after having burned the internal parts it kindles up a fresh inflammation on the external surface, and most frequently the horrible fire visible manifests itself first in the face, but sometimes, on the contrary, it begins on the elbow, knee, and the joints, as well as on the feet and hands. Persons thus attacked have no hope of cure, because the physician, by carelessness or ignorance of the true nature of the disease, does not apply his art when the first symptoms appear.

"The patients are dull, taciturn, drowsy for a time, and suffer from constipation, but all of these symptoms are not of themselves

extraordinary, for they occur in people otherwise healthy. When the disease has made progress, the breath becomes fetid on account of the internal decomposition of the vital forces. The urine becomes thick, white, frothy, like that of a beast of burden. The patients digest without difficulty raw food, and do not appear to observe whether the digestive functions are affected. The loss of digestion in them is not noticed, for though in general they receive no benefit from the food, digestion appears to be easy, as if the disease devoured food for its own sustenance.

"Tumors arise one by the side of another, not continuous but thick and unequal. Amongst the tumors there are fissures as in the skin of the elephant. The veins are increased in volume, not by abundance of blood, but by the thickness of the integuments. The hairs for the most part die. They become scanty on the thighs, calves of the legs, groin, and on the chin. The hair of the head becomes thin, gray, and a rather pronounced baldness appears prematurely. Soon the crown and chin are completely denuded of hair, and if any remains, however little, it serves only to disfigure the patient. The skin of the head is deeply wrinkled. More prominent tumors appear on the face. They are sometimes white at the summit, but greenish at the base. The pulse is feeble, heavy, slow as if moved with difficulty.

"The vessels in the temples and under the tongue are swollen. The stomach is filled with bile. The tongue becomes unequal on account of granular nodosities, and it is not surprising to see the whole body covered with similar nodules. But if the disease develops rapidly in internal parts and shows itself on the extremities, lichenous eruptions develop which sometimes surround the chin in a circle. The cheeks become red and swell a little. The eyes are dark and copper-colored; the eyebrows prominent, thick, bare, and overhanging. The space between them is contracted. The color is leaden gray and blackish. The lower part of the frontal skin is drawn downwards and conceals the eyes, as in mad persons and lions. This is why the affection is also called *leonine*. There are dark tumors on the nose, which is pointed and prominent. The lips are thick, the lower one being blue-back in color. The teeth are destitute of whiteness and are blackish. The ears are red, but inclined to become black, the apertures are apparently larger than usual, and at their lower parts there are ulcers from which flows a very pruriginous matter. There are also upon the whole body wrinkles, deep incisions as well as furrows. This is why the disease bears also the name of *elephantiasis*.

"The soles of the feet as far as the middle of the toes are cracked.

If the disease increases, the nodosities of the cheeks, chin, fingers, and nose become ulcerated. These ulcers are fetid. They are incurable and appear in continous succession. Sometimes the limbs perish before the individual, and at last there is seen to fall the nose, the fingers and toes, feet, hands, and genital parts, for it is only after the patient is dismembered that the disease causes death as a deliverance from a horrible life and fearful sufferings. But this affection has the same tenacity of life as the elephant. The taste is lost. Neither eating nor drinking gives pleasure to the patient.

"In consequence of their sufferings they have an aversion to everything. They abstain from food and have a strong inclination to sexual appetite. Languor is manifested. Weakness is particularly revealed in every limb, and even the small members are a burden to the sufferer. The body finds everything repugnant. It does not feel satisfaction either in the bath or in abstinence from it, eating or fasting, exercise or repose, for the malady is in enmity with everything. Sleep is insignificant. Watching is worse on account of hallucinations. The respiration is greatly disturbed. The patients often feel, as it were, strangled with a cord. Some thus finish a remnant of existence in sleeping, a sleep from which there is no rising until death occurs. Such being their condition, who can avoid flying from them? Who will not turn away from them, were it even his father, or son, or own brother? There is also the fear that the disease may be communicated. Many for this reason remove their dearest ones to solitude or to the mountains. Some preserve them from hunger for a time, others not at all, desiring their death."

Arabia.

There is no authentic historical evidence of the existence of leprosy in Arabia before the time of Mohammed, although from its known prevalence in Egypt and Syria from the earliest times the close communication between these countries and Arabia would render it probable that the disease was carried to Arabia at an early period. Kaposi gives a long list of Moorish and Arabian writers who have produced treatises on leprosy, partly borrowing from the Greeks and partly basing their descriptions upon their own observations of the disease.

Italy and Continental Europe.

According to Aretæus, it had in his time begun to spread into Western Europe. The Romans acquired leprosy after the Greeks. Celsus, Galen, and Pliny thought that it was imported into Italy by

the troops of Pompey and that leprosy had gained Italy about one century before Christ. Henceforth its spread was rapid over Europe. We can trace it into France, Spain, Great Britain, Germany, Russia, and Scandinavia. We find it rising and declining at different periods and in different parts of the world, moving gradually from east to west and from south to north. While it is found prevalent in Egypt and India in the early period of the world's history, in the beginning of the Christian era it spread through Greece and Southern Europe during the period ranging from the sixth to the seventh centuries, reaching its culminating point during the crusade in the eleventh and twelfth centuries, and began to decline from the fifteenth to the seventeenth centuries.

The traditional idea that leprosy was introduced into Europe by the crusaders is without foundation. It prevailed extensively in Western Europe long before the crusades were instituted, although there is no doubt that the movements of the crusaders to and fro afforded effective means for the further spread of the disease. Certain writers have attributed its introduction into Western and Eastern Europe from Asia Minor to other agencies. Simpson suggests it may have been brought by Roman armies or by numerous pilgrims who were accustomed to flock to Jerusalem from various parts of Europe. Even before the foreign armies left Britain in 418 numerous pilgrimages had been made to Jerusalem. There were abundant opportunities for contracting the disease in Jerusalem, where it had existed from time immemorial.

Great Britain.

The early history of leprosy in Great Britain has been studied with great care by Sir James Y. Simpson. He regarded it as probable that leprosy was introduced into Great Britain by processions of pilgrims to the Holy Land going and returning through Italy; the opportunity for contagion being afforded in both these countries. The pilgrimages to the Holy Land were of frequent occurrence, and the conditions of travel at that time necessitated the close contact and intimate relations which favored the communication of disease.

Newman also has made an admirable study of the "History, Decline, and Final Extinction of Leprosy as an Endemic Disease in the British Islands." His researches prove that leper hospitals existed in Ireland and that leprosy was prevalent in England long before the first Englishmen engaged in the crusades. The disease spread more or less rapidly through England, Wales, and Ireland, although it always prevailed more extensively in certain localities

than in others. It was very prevalent in the twelfth, thirteenth, and fourteenth centuries, as shown by the number of leper houses that existed and by the ecclesiastical and legal regulations that were promulgated in respect to them. The disease was also common in the fifteenth and sixteenth centuries, but had then begun to decline. During the reign of Edward VI. (1547–1563) it was reported by a commission that most of the lazar houses in England were empty.

It is not known at what precise period leprosy was first introduced into Scotland, but the general impression is that it was a century or two after its introduction into England. The earliest lazar house in Scotland dated back to 1150. Numerous lazar houses were established in various parts of the kingdom during the next two or three centuries. The decline of leprosy in Scotland was noticed in 1652 by an act for the diminishing of the houses at Edinburgh, but the disease still prevailed in the islands to the north of Scotland and in the Shetland Islands. In 1742 a public thanksgiving was ordered for the permanent disappearance of leprosy from the Shetland Islands. The last leper of the Shetland Islands, it is stated, died in the Edinburgh Infirmary in 1798.

The disease began to disappear in France and Italy at the end of the sixteenth century, although leprosy centres were found on the south Mediterranean coast in the seventeenth century.

In Norway there is a record of the establishment of a leprosy hospital at Bergen in 1276, and the number of lepers was found to be increasing in 1745. A leper hospital was established in Austria in 1301 and in Sweden in 1248. Evidence is abundant that leprosy was present in Denmark.

Leper hospitals were also established in Iceland in the fifteenth and sixteenth centuries.

North and South America.

In America the history of the introduction of leprosy and its spread in the British provinces of North America, the United States, and South America cannot be definitely traced. There are no authentic records of its existence in New Brunswick until 1815. It was introduced into Louisiana by the Acadian refugees who were deported from Nova Scotia.

In South America leprosy was introduced by the French, Spanish, and Portuguese settlers, with an added increment of infected material from Africa, the East Indies, and elsewhere.

Kubler, in his remarks upon the geography of leprosy, suggests that there is some connection between leprosy in America and Africa,

as the countries most occupied are on the side looking towards Africa. A question of some importance in this connection is that of pre-Columbian leprosy. Dr. Ashmead has made a very careful and elaborate study of pre-Columbian leprosy, in which he has examined collections of the pottery found by the sides of mummies, the hands and feet of mummies from Peru, from Chihuahua, North American Indian remains, and from Mexico, and various other presumably prehistoric remains from numerous other localities. In none of these bones was there any evidence of leprosy. Nor were there any deformities depicted on the American pottery which could be identified as characteristic of leprosy.

Within recent times leprosy has been widely disseminated in the far East and in the islands of the Pacific chiefly, it is generally held, by the Chinese. Cantlie declares that "the Chinaman taints the world with leprosy," and he brings forward historical evidence to prove that the spread of leprosy in the Malay peninsula, the Dutch, Spanish, and Portuguese East Indies, and in Oceanica, as well as the islands of Fiji, New Caledonia, Hawaii, and the western coast of America, may be traced to Chinese coolie immigrants. "The Chinamen are not only the probable introducers, but the chief victims. With the exception of Hawaii and New Caledonia, all over Indo-China, Malaya, the Indian archipelago, and the Pacific it is the Chinaman who is the dominant leper."

Whether these Bohemians of the Orient have carried leprosy with them in their world-wide migrations, or whether they simply serve as scapegoats, the opinion generally prevails that they have been the chief contaminators of the world with leprosy in modern times.

The following chronological table, which gives the chief dates in the history of leprosy which has been compiled from the most authentic sources accessible, is taken from the prize essay, "The History of the Decline and Final Extinction of Leprosy as an Epidemic Disease in the British Islands," by George Newman, 1895. The writer has supplemented it with a few dates, while omitting many details relating to the leper houses in Great Britain which are of less general interest:

Chronological Table of Leprosy.

B. C.

3500. Leprosy in Egypt (Husapti?).

1320. The exodus.

1000–900. Celts in England.

600–400. Leprosy common in Hindoostan (Susruta) and China.

460. Hippocrates described leprosy.

260. Manetho testified to presence of leprosy among the Jews (90,000).

200. Leprosy common in Greece, called elephantiasis (Kaposi).

100. Leprosy known in Italy.
95. There is a disease called elephas which has its rise on the river Nile in the middle of Egypt (Lucretius).
60. Leprosy first in Spain.
53. Celsus wrote on leprosy.

A.D.

81. Aretæus wrote on leprosy; also in second century (?).
97. Archigenes wrote on leprosy also.

Second century. Leprosy became prevalent in Europe between the second and the sixth centuries.

Fourth century. Theodoret mentions lazarettos for lepers.

360. Oribazius wrote on leprosy.
366. Order of St. Lazarus founded in Palestine.

Fifth century. Actius wrote on leprosy, describing it as widespread.

432. First notice of leprosy in Ireland (Colgan's "Acta Sanctorum").
500. Charaka wrote on leprosy.

Sixth century. Gregory of Tours speaks of lazarettos.

549. Council of Orleans leprosy decree.
550. Pestilence of leprosy in Ireland ("Chronicon Scotorum").
583. Council of Lyons leprosy decree.

Seventh century. Hospital St. John founded for lepers (Lake Constance). Leper houses existed at Verdun, Metz, and Mastricht (Virchow).

603. St. Kentigern, of Glasgow, died: "mundabat leprosos."
606. Increase of leprosy during a Roman invasion in the time of Heraclius (Lanigan, "Eccles. Hist.").
661–664. Leprosy in Brittany.

Rothar, King of Lombards, made laws to prevent the marriage of lepers.

Pestilence depopulated Britain and Ireland.

Eighth century. St. Boniface "mundabat leprosos." Hospital St. Lazarus founded at St. Gallen, Lake Constance, 720. St. Othmar founded leper houses in Germany (died, 758). St. Nicholas of Corbie founded leper houses in France. Isidore of Spain alludes to leprosy in Spain.

757. Pepin provided an act that leprosy should be sufficient cause for separation or divorce (Parliament at Compiègne).
789. Charlemagne re-enacted similar laws; also enforced sequestration.
868. Council of Worms leprosy decree.
869. Leper hospitals existed in Ireland. The hospital at Armagh burned by Arlaf.
874. Iceland peopled from Norway.

Tenth century. Leprosy prevalent in Europe; in England. Leper laws, Venedotian and Dimetian codes. Law was passed in England making leprosy a cause for divorce.

928. Truela, son of King Alfonso of Spain, dies of leprosy.

Leper houses had existed in Palestine for nearly a thousand years.

950. Hywel Dda, or Howell the Good (a Welsh king who died about 950), enacted a code of laws relative to leprosy ("Celtic General Repository," vol. iii., 199).
958. Leprosy mortality excessive. Suffering and misery throughout Europe.

1007. Leprosy prevalent in Spain. In this century first leper hospitals and pest houses were built.
1067. First leper hospital in Spain (Valencia).

1075. Hugh D'Orivalle, Bishop of London, had leprosy.
1084. Several leper hospitals founded in England previous to first crusade.
Leper hospital founded at Canterbury by Lanfranc (Archbishop of Canterbury), who died 1089.
1095. First Crusade begun by Peter the Hermit.
1098. Return of the first Crusaders. Low condition of English agriculture, misery, famine, and pestilence.
Twelfth century. It was a custom before this century to burn and otherwise persecute lepers in Europe. Henry II. in an edict sanctions it in England. The writ "De Leproso Amovendo" in force at this period. The earliest mention of leper houses in Scotland. Knights of St. Lazarus acquired a footing in England (Stephen). Leprosy prevalent in Denmark (Gislasen). Third crusade under Richard I. Baldwin I., King of Jerusalem, became a leper and ten years later resigned his crown because of disablement (1184). Founding of numerous leper houses in England and Scotland (first in Ireland, 1165). Over fifty leper houses.
1179. Council of Lateran, famous leprosy decree.
1181. Pope Lucius III.'s leprous decree.
1190. Pope Clement III.'s leprous decree.
1192. Famine in England. Approximate time of appearance of leprosy in Iceland.
1200. Leprosy decree of Provincial Synod at Westminster; Hubert, Archbishop of Canterbury. Henry III. visited lepers every Holy Thursday.
Thirteenth century. Leprosy reached its zenith during this century (Liveing) (?). Period of returning Crusaders. Louis VIII.'s code of French leper laws. Two thousand leper hospitals in France. Equal number in middle of fifteenth century (Heren).
1242. Leprosy canons of Scotch Church, separating lepers from society.
1248. Ferdinand III. founded leper hospital at Seville.
1250.* Leprosy existed in Japan.
1263. Norwegians invaded England, and in 1266 first mention of leper houses at Bergen, Norway.
1269. Leprosy segregation of the canons of the Scotch Church.
1270. St. Louis of France on the last crusade. Many of his soldiers became leprous (Joinville).
1283. Statutes of Society of Merchants ordered that lepers should not come into the burgh.
1290. Council of Nogaro exempted lepers from the jurisdiction of secular justices, prohibited their entrance into markets or towns, and insisted on their wearing some distinguishing badge.
1296. Leprosy in Edinburgh. Fifty leper hospitals built in thirteenth century. Leprosy prevalent, but probably declining.
A leprosy "visitation" in the west of England (Somerset, etc.).
Fourteenth century. Commencing decline of leprosy throughout Europe during this century. Numerous leper houses built in England and Scotland. Lepers getting scarce at various places. Leprosy visitation in west of England. Regulations against lepers entering city of London.
1350. Lepers getting scarce at St. Albans and Aylesbury.
1357. Black Death in Europe; in England 1349. Laws passed in England protecting fishers and for the supply of fresh fish instead of dried. Laws passed against water pollution. 1389, cleansing the streets.

1365. There were now four leper houses at York, and they remained for just one hundred years (Robertson).
1375. Regulations against lepers entering the city of London; the taking of the oath by John Gardener.
1389. Renewal of persecution of lepers in France (Charles VI.).
1398. John of Gaunt's will, bequeathing to London lepers. Henry IV. a leper (according to Gascoigne).
Fifteenth century. 1407. Great plague in London. Numerous leper houses provided in Switzerland and Spain.
1413. St. Mary Magdalene Hospital at Reading closed because no lepers forthcoming.
1414. Leper hospitals in England "for the most part decayed, and the goods thereof spent in other use" (2 Hy. V., c. i.).
1427. Scottish Parliament compelled to legislate for lepers (1427, c. 8, ii., 16).
1468. The leprosy certificate of the court physicians of Edward IV.
1470. A royal commission, appointed by Edward IV., reported marked decrease of leprosy.
1485. Lepers still in London, and a number of legacies left to them ("Calendar of Wills," vol. ii.). Leprosy by no means rare in Lincolnshire.
Sixteenth century. Leper hospitals still being founded in Netherlands and parts of Germany and Spain. Final extinction of leprosy in Denmark (Gislasen.)
1536–1540. Suppression of the monasteries and many of the existing leper houses; but the larger ones were spared by Edward VI. (c. 3), "to prevent the contagion spreading." A royal commission (Edward VI.) reported most of the leper hospitals in England empty, 1547. Leprosy was frequent in Cornwall in the time of Elizabeth (Polwhele).
1542. Leper hospital built on Canary Islands.
1555. Leprosy very prevalent in Iceland.
1574. Herbaldowne Hospital providing relief for more than thirty. Leper laws made in Scotland; repealed, 1579.
1582. Refoundation of Bodmin Hospital by Elizabeth. "A great company of lazar people." Glasgow lepers allowed free access to burgh (Robertson) till 1593.
1585. Sherburn leper hospital, diverted from its original purpose (because no lepers were forthcoming), became a general hospital.
1591. Five lepers consigned to hospital in Edinburgh. Lepers still at Aberdeen. Apparent outbreak of leprosy in Scotland.
1593. Glasgow lepers banished from the burgh by Kirk Session.
1598. Heutzner, travelling through England, remarks on the frequency of leprosy. Thirty-nine lepers in Bodmin Hospital in James I.'s reign, who were largely patronized by the king.
Seventeenth century. Four leper hospitals built in Iceland, 1651.
1652. For "many years Ireland hath been almost quite freed" from leprosy (Boate).
1656. Leper hospital built in Madeira.
1657. An order made to dismantle the lazar house at Greenside, Edinburgh.
1661. Leper house at Aberdeen razed to the ground. Leprosy was prevalent in the Faroë and Shetland Islands.
1676. Leprosy very prevalent in the Faroë Islands, Shetland Islands, St. Kilda, 1684.
Eighteenth century. 1707. Smallpox epidemic in Ireland killed one-third of population, including many lepers. Leprosy still in France (Upper Auvergne, etc.), Belle Isle still used as leper refuge.

1730. Leprosy prevalent in Ireland (Von Triol).
1749. Public thanksgiving in Shetland on account of disappearance of leprosy (few cases still appear).
1753. Several lepers in St. Kilda.
1759. One hundred and fifty lepers in Norway (three hospitals).
1768. Two hundred and eighty lepers in four Iceland hospitals (Petersen).
1769. Captain Cook landed in New Zealand. Leprosy present (?).
1775. Last endemic case of leprosy in Ireland at Waterford.
1778. "A leper is now a rare sight" (White of Selborne).
1787. Leprosy endemic in Auvergne.
1798. A man, John Burns, a Shetland leper, descended from a leprous family, admitted into the Edinburgh Infirmary.
Nineteenth century. Leprosy unknown as indigenous disease throughout the British Islands. Since 1882 twenty cases of leprosy have been brought before London Dermatological Society, probably none were indigenous.
1809. Supposed case of indigenous leprosy in Edinburgh; another in the Shetlands (Edmonston).
1810. Leprosy endowment in Cornwall transferred to general infirmary because there were no lepers needing assistance (Brown's "Cases in Chancery," 166, n.).
1811. First leprosy hospital at Calcutta.
1815. Leprosy in New Brunswick.
1836. Many lepers still in Norway and Iceland. Some in Portugal, Spain, Italy, Sicily, Crete, New Zealand, etc. Very prevalent in India, China, Japan, and the West Indies.
1848. Leprosy introduced into Hawaiian Islands.
1850. Beginning of leprous endemic in Parcent, Spain.
1863. Leprosy still common in Iceland.
1866. Beginning of leprosy endemic in Louisiana.
1867. Royal College of Physicians Report declaring leprosy non-contagious.
1868. Leprosy introduced into New Caledonia
1874. Leprosy bacillus discovered by Hansen.
1885. Norway contained 1,377 lepers.
1889. Six hundred lepers at the Cape of Good Hope.
1890. Disease practically extinct in New Zealand; 18,000 lepers in Colombia.
1892. Lepers in Spain, 1,200; Norway, 1,200; 600 to 700 elsewhere in Europe. Lepers in India, 100,000; Japan, 150,000 (?).
1894. Iceland, 140; 1897, 200.
1897. Berlin Leprosy Congress.

Methods of Dealing with Leprosy in Ancient and Modern Times.

Isolation of Lepers.

It is to be understood that a broad signification is given to the term "isolation" in this connection: it will be used synonymously with segregation or compulsory gathering together of lepers.

Complete isolation of lepers is practically impossible; even in countries where leper hospitals and asylums have been established strict isolation of the inmates does not exist. They come more or less in contact with physicians, nurses, clergymen, attendants, and purveyors of their food and other supplies, so that no leper community can be absolutely shut off from the world.

In all ages and in almost all countries mankind has waged a relentless warfare against the leper. The belief in the contagiousness of leprosy which was universally held from the earliest ages until within recent times has led to an avoidance of contact with those afflicted with the disease, and in most countries there has been a general tendency to ostracize or segregate them. All the severe proscriptive measures formulated in the Levitical code and those practised in the Middle Ages were based upon the belief that the leper is a source of danger to those with whom he may come in contact. Even in countries where segregation is not prescribed by legislative enactments or enforced by governmental authority, public sentiment has restricted association with lepers.

In India, China, and Japan, which are among the oldest leprosy centres of the world, public opinion has decreed that those affected should withdraw from the society of their fellows and dwell apart. To this prevalent sentiment may be traced the origin of the leper villages and leper homes which form so distinctive a feature in many Oriental countries, especially in China.

There is no doubt that the attitude of public sentiment towards lepers is modified by race, religion, and civilization. Among certain races—the negroes of South Africa, the Kanakas of New Caledonia and of Hawaii—leprosy inspires neither disgust nor fear.

Dr. Ross says of leprosy in South Africa: "It is a singular fact that the people among whom leprosy is spreading have no fear of contagion among themselves, nor do they abstain from embracing or handling each other. The disease, so repellant to Europeans, seems to have no repulsion to them. They bitterly resent being parted from their kith and kin."

In an article, published in 1889, embodying my observations of leprosy in Hawaii, I wrote: "The Hawaiian, be it understood, has not the wholesome horror of the disease entertained by his more civilized brothers. He ignores its contagiousness, and neither disgust nor fear leads him to shun his brother leper as a bearer of deadly contagion. Leprosy carries with it no social ostracism and arouses no instinct of self-preservation on the part of the patient's friends. It is this total absence of fear, this ignorant contempt of its contagiousness combined with the promiscuous and intimate intercourse

between the healthy and the diseased which accounts for the rapid and unexampled spread of the disease in these islands."

Dr. Le Grand bears much the same testimony as to the attitude of the natives of New Caledonia towards those affected with the disease.

Among Mussulmans leprosy does not spread with the same rapidity because it inspires a fear or terror which prompts every person to avoid contact with a leper, except he happens to be a member of his own family.

In the Isle of Mytelene, Zambaco Pacha declared that in a population of several thousand Mussulmans there was not a single case of leprosy, which he attributes to their wholesome horror of contact with the disease.

The natural affection existing among members of the same family has proven to be the most formidable obstacle to the segregation of lepers. This sentiment of affection protests against the casting out of a member of a family until the disease becomes so disfiguring as to be repulsive, and this in connection with the opportunities of contagion inseparable from family life, is probably the explanation of why leprosy is so essentially a family disease.

It has been generally supposed that the Jews were the first to segregate lepers. It is known, however, that the Persians had laws for the extermination of leprosy before the time of Herodotus. This author states (edition Feubrini, chapter 138): "If any citizen has lepra or leucé, he may not enter into the city or mingle with the Persians. Every stranger who is attacked is exiled from the city."

It is probable that segregation was practised in other countries where leprosy prevailed. It has been suggested that Moses, in separating lepers from the healthy and compelling them to dwell apart, followed the custom he had seen practised in Egypt. In any case, the policy of the segregation of lepers has been perpetuated with varying degrees of severity and strictness from Mosaic times to the present.

During the great epidemic of leprosy in Europe in the Middle Ages the practice of segregation was prosecuted with the greatest rigor.

Reference will be found in the section on geographical distribution of leprosy to the barbaric practice prevalent in many countries of the putting to death of lepers or banishing them in the forests and deserts to die of hunger and exposure.

In China, according to Cantlie, it has happened that when a case of leprosy had declared itself the parents, after having drugged the patient, burned him alive.

Segregation has been sanctioned by the experience of centuries as the best prophylactic measure against the spread of leprosy.

The Levitical code decreed that the leper should be cast out of the city and transported to a place called Beth Chofschitch, which means "houses of impurity." Not only the leper, but his habitation, was declared to be unclean. Jewish lepers under the penalty of eighty stripes were forbidden to approach the mountains of the temple, yet were not rigidly condemned to isolation, and in towns without walls were even allowed to enter synagogues. They were required to make themselves known at the first glance by appearing in public with rent garments, bare head, and covered beard, and if any one approached inadvertently the lepers were to cry, "Unclean, unclean!" They were interred in a separate burial ground (Thin).

We have little definite knowledge respecting the measures of dealing with lepers before the invasion of Europe by the disease. Reference has already been made to the extent to which leprosy scourged the population of Europe between the tenth and sixteenth centuries. We know that during the period of this great epidemic the church and State united their immense authority to secure the isolation of the lepers.

According to Dr. G. Contenau, who has made a special study of the prophylaxis of leprosy in the Middle Ages, the leproseries in France were composed ordinarily of low buildings, without ventilation, enclosed by walls, with gardens, wells, chapel, and chaplain in most of them. They were always designated by the name of a patron saint. In France they were under the protection of St. Lazar, of St. Marthe, or St. Madeleine. In Central Europe they were under the protection of St. Jaques. In the north and east of Europe St. George was the patron saint, and in Poland St. Valentine and St. Leonard.

"They were ordinarily situated near a cathedral without the walls of a city. They were built at the expense of the king or of the city or often by charitable private means. They were supported often by the crown almsbag, which was made up of receipts from the rich lepers. The excess of these receipts was divided among the poor. Often the leproseries had revenues in silver or in wine, barley, etc. Although in the hospitals in the Middle Ages there were four or five patients in the same bed, and oftentimes as many upon the roof, the proportion of the lepers was always restricted in these leproseries on account of their immense number. When an individual was recognized as leprous, his admission was gratuitous (by the grace of God). If he was rich, he brought his house utensils and a sum varying from ten to fifteen pounds sterling. The leprosery was ordinarily under

the charge of a master or superior, assisted by leprous brothers and sisters. Sometimes the chaplain was the chief, or instead a leper was elected provost by the lepers. The ceremony of the entrance in a leprosery was as follows:

"The priest with a cross went to search the leper, conducted him personally to the church where he held mass, under the cloth of the dead. At Amiens as a sign of renouncement of the world the leper lay for a certain period in a grave. By his admission the leper lost his civil rights. He could neither devise nor possess. His marriage was annulled. If he had children of tender age, they were separated from him, to avoid contagion, but his wife might remain with him if she wished.

"He received a gray calemot, a great coat, a claquet to warn persons of his presence, a hood, and a sort of scarlet epaulet.

"The lepers were compelled to wear a visible sign by which they might be distinguished. No inmate of a leper hospital was allowed to enter the town of Castres unless he had a white cloth around his neck and a claquet, or rattle, with which to make a noise to warn people of his approach. A high sack or a hood was also part of his vestment. Not only the lepers, but those in charge of them, were compelled to wear some dress of distinctive mark.

"The members of the grand Betra establishment of lepers were compelled to wear on their dress a capital L of red cloth, one-half a foot long, over the left breast, and this because they were in frequent contact with lepers and might communicate the disease.

"Both male and female lepers took the name of brother and sister and lived in community. They were compelled to receive communion, hear mass, live purely and chastely; their expulsion was the consequence of grave infraction. The leproseries had then a religious character; they were of a true monastic order by compulsion, it is true, and not by volition. But it should not be forgotten that in the Middle Ages the monastic state was regarded as enviable.

"The lepers had their subsistence assured. They had money for their small expenses. They were not submitted to claustration. In the regulations of the leproseries there were disciplinary measures; the most severe was expulsion. The leprosery was not then an inferno, as in that case the expulsion would not have been considered a chastisement. The best evidence of this is the considerable number of false lepers which it was necessary to evict."

Ambroise Paré has reported the history of an unfortunate tubercular leper, whose ulcers were simply painted to insure his entrance. This practice of simulation, almost incredible as it may appear, is by no means extinct. In my observations of leprosy in the Sandwich

Islands I found that occasionally natives from one motive or another, sometimes to join their friends or family, will endeavor to simulate the disease in order to be sent to the leper settlement. With an irritant they will produce discolorations of the skin which resemble the port-wine discolorations characteristic of the beginning stage. This is often most artistically done, and the simulation is most deceptive.

In consigning a leper to the leprosery an examination was made by a jury consisting, at Laon, for example, of a doctor, a surgeon, and an apothecary.

The signs of leprosy were divided into univocal and equivocal. According to Chauliac and B. de Gordon, the univocal signs were "roundness of the eyes, loss of the eyebrows, dilatation of the nostrils, with narrowness of the summit, a raucous voice, alteration of the lips, the fixed regard of the satyr (the beast of horrible aspect in which are the said signs)."

The equivocal signs were "tuberosities of the flesh, the color of morphœa, atrophy of the muscles, stupor and insensibility, creeping of the flesh. The blood is black, granular, salt clings on the skin of the leper, water adheres to it like oil."

Ambroise Paré thus describes the method of examination made by a jury of surgeons, of which he was a member, to ascertain if X. was a leper (1583). The report is as follows: "In the first place, we found the color of his visage blotched and pimpled and full of bluish spots, then we plucked hairs from his beard and his eyebrows and found that a small portion of flesh was attached to the root of the hair. In the eyebrows and the lower part of the ears we found small tubercles, the brow wrinkled, the expression fixed and immobile, the reddish eyes flaring, the nostrils enlarged without and contracted within, as if obstructed with small encrusted ulcers, the tongue swollen and black, and above and beneath we found thin small grains as one sees in measly pigs, the gums corroded, and the teeth denuded, and the breath offensive, having a rough voice, speaking through his nose. We also saw him naked and found the surface of his flesh rough and unequal, like that of a thin-plucked fowl, and in certain places many dartres. Besides we punctured profoundly with a needle the tendon of the heel without his feeling pain. By all these signs, unequivocal and equivocal, we declared that X. is a confirmed leper."

So rapid was the increase of leprosy that in the time of Louis VIII. there were in France two thousand leper houses, and the number in Europe, without counting those in Russia and Sweden, was nineteen thousand.

In England, Scotland, and Ireland isolation was enforced and rendered possible by the multiplication of lazarettos all over the country. The church regarded the leper dead, and performed the burial service for him on the day he was separated from his fellow-creatures and confined in the lazaretto. The priest went with the cross to the house of the condemned leper, and consoled him for the incurable plague with which God had stricken him, and then the condemned was conducted to the church, the usual burial hymn being sung on his way thither. The parents, friends, and neighbors joined in the hideous cortège which rendered the last honors to this living cadaver. Upon reaching the church, he was clothed in a funeral pall, and while placed before the altar between two trestles the mass for the dead was celebrated over him. After this service he was again sprinkled with holy water and led to the house or hospital destined for his future home, where he was compelled upon entering to take the vows of obedience, poverty, and chastity. A pair of clappers, a stick, a cowl, and a gray habit were given to him.

Before leaving the leper the priest solemnly forbade him to appear in public without his leper's gown to warn people who did not know him to flee his company, or to enter inns, mills, churches, and bakehouses. He was forbidden to enter any inn or habitation other than the one in which he dwelt, and when he wished wine or meat it was brought to him in the middle of the street, or to touch children or to give them what he had touched, to wash his hands or anything pertaining to him in the common fountains or streams, or to drink from them except in a special cup, to touch in the market the goods he wished to buy except with his stick, and in asking alms he was always to sound his rattle; he was forbidden to eat or drink with any other than lepers, and especially to walk in narrow paths or to answer those who spoke to him in the roads or streets, lest he should infect those whom he might meet by his pestilential breath and with the infectious odor which came from his body. Before leaving the leper forever to the seclusion of the lazar house the priest terminated the separation from his fellow-creatures by throwing upon the body of the leper a shovelful of earth in imitation of the closure of the grave.

Upon the death of the leper his habitation was burned, and he himself was buried with his face to the earth. In many places the corpses of lepers were found in this posture.

Dr. Newman, in his prize essay on leprosy, refers to many curious laws relating to the lepers in England and Scotland. He characterizes them as curiously contrary and extravagant, some being so mild and indefinite as to be useless, others so strict and severe as

to be cruel and impossible to keep, and concludes that "strict segregation as understood and practised nowadays never entered the minds of those desiring to separate lepers from the healthy."

The religious duties forced upon inmates under the control of the church were of the most monastical character. During Lent all the brothers as well as sisters were obliged to receive discipline three days in the week. Disobedient members were punished at the discretion of their prior and prioress by corporeal correction, and offenders who refused to submit to the usual discipline were reduced to bread and water, and after the third offence they were liable to be ejected.

No inmate was allowed to transgress the bounds or to attempt to go beyond the walls of the hospital without his close cape, or to stand or walk by any king's road before or after service. By a decree of the Archbishop of Canterbury (1200) lepers, when forming a large colony, were entitled to have their own church and graveyard, but in many places this special church and graveyard were quite impossible through lack of funds and lack of lepers. In many places arrangements were made by which the lepers were enabled to take some share in the church services by means of the leper window or squint window or hagioscope. There were generally openings or apertures in the wall or narrow, oblong slits through which the elevation of the Host at the high altar and other ceremonies might be viewed without the lepers themselves being seen by the congregation. Certain churches also had a stone slab let into the sill of the window and so placed that a leper could receive the sacrament without actual contact with the administrator.

By the laws of England lepers were classed with idiots, mendicants, outlaws, etc., as incapable of being heirs.

In both Britain and Normandy lepers were expelled from society, and had no power to alienate their effects or dispose of them to any one. They were regarded as dead.

It would appear that the means provided for the sustenance of the lepers were not of a very abundant character. The lepers were allowed to go where they chose and beg what they could or reside in any leper hospital to which they could get admittance.

A regulation in support of the hospitals all over the land states that tainted beef is to be sent to the leper house in the neighborhood, and if there was not one, then it was to be destroyed. Then again, when a wild beast was found wounded or dead in the forest it was to be sent to the nearest leper hospital.

Many hospitals were supported by voluntary or compulsory contributions of a certain toll upon everything carried to the markets.

Other establishments were financed by means of fairs in which the chief articles for sale were wool, meal, hops, hardware, etc., and on one day horses. The business transacted was very extensive.

In the hospital at Edinburgh it seems that the lepers were kept in the home, and between dawn and sundown the lepers took turn in sitting at the gate asking alms, which were put in their cups. The allowance was only four shillings a week for each inmate.

At the hospital in the city of Glasgow the inmates were allowed to go out of the hospital, drawing attention by means of their clapper, and asking alms.

The number of leper houses in England, Scotland, and Ireland was over two hundred. "The number of these lazar houses, however great, was insufficient to accommodate more than a small proportion of those suffering from the disease."

In a majority of these leper houses, if a man was married, the wife was allowed to go with him. As early as 789, Charlemagne promulgated laws forbidding the marriage of lepers. A similar law was passed in Great Britain by the Welsh king, Hywel Dda, who died in 950, and there are acts of Parliament which forbid cohabitation if either wife or husband is a leper, the leper in these circumstances being considered as dead.

In 1757 leprosy was declared to be a valid cause for divorce in France. In 1776 a law was passed in Iceland to prevent lepers from marrying.

As early as 1488 there was an edict ordering all lepers to leave Paris.

In England in the fourteenth century, according to Simpson, a leprous woman with a child was buried alive, and in 1746 lepers were driven from London.

The harsh measures used in Europe for the suppression of leprosy have always been regarded as an illustration of the value of segregation. Strict segregation, if we are to trust to historical evidence, was, however, never carried out, as the inmates of most of the leper homes were not strictly confined, but were allowed to leave the hospitals and beg in the street, and thus mingle with their fellow-beings.

Nevertheless leprosy decreased in a most remarkable manner. In the thirteenth century the disease reached its zenith in Europe. In the fourteenth century it had commenced to decline throughout Europe, and by the end of the sixteenth century it had practically disappeared.

Dr. Newman is inclined to attribute the decline and final extinction of endemic leprosy in England and Scotland, not to segregation, but

to the tendency of leprosy to die out under the more favorable hygienic conditions, good food, and improved sanitation.

It is stated that formerly in China more drastic measures were used for the suppression of leprosy than now prevail.

Dr. B. Taylor, of Fuh Ning Fuh Chow, in China, states that, while there are lepers in the vicinity, there are none in the town itself, and that in a small village a mile from the city a village hospital still exists, but there are no lepers in it. Concerning this assertion Dr. Taylor has been told that a mandarin, about sixty years ago, desirous of stamping out leprosy, having invited all the lepers to a feast in the hospital, surrounded it with soldiers and then set it on fire.

Richard, in his history of Tonquin, states that leprosy is so common in Tonquin that there are pieces of land assigned where those attacked by it must reside. They are shut out from society, and it is even lawful to kill them if they enter cities or towns.

In Damascus the fear of detection is stated to have compelled lepers either to live in communities in huts outside of the village or to seek refuge in leper houses in the city.

In comparatively recent times a leper house has been discovered in Bagdad surrounded by a thick wall, with a little room in which all the lepers were compelled to retire.

In Rhodes they are said to have been banished, destroyed, or sent to some uninhabited island to subsist as best they could.

In Finland lepers were at one time isolated in houses built on islands in the lake, and on the death of the leper the house and all its furniture were burned. Similar leper huts were found by Savory in Candia, and Boeck discovered them in the island of Siera.

In Europe the leper houses were abandoned because of the gradual decrease and final extinction of the disease, but it is worthy of note that in other countries leper houses and hospitals have fallen into disuse or been abolished from indifference on the part of authorities or from a lack of confidence in their utility. For example, in Iceland towards the middle of the sixteenth century four leper houses were erected in four quarters of the island. In 1848 the leper hospitals were abolished. It is worthy of note, however, that during the past year (1898) a leper hospital has been built at Reikiavik.

In various portions of China, in Java, as well as in North and South America, lazarettos which were formerly used for the isolation of lepers have fallen into disuse. The San Lazaro Hospital, which was founded in Mexico by Cortez, the conqueror, was abolished about thirty-five or forty years ago, although there has been no sensible decrease observed in the disease.

The decline of the epidemic of leprosy in Norway is cited as an

evidence of the value of segregation. Since the establishment of the leper hospitals 3,400 lepers have been admitted, while during the same period 5,053 new cases have appeared. The total number of known lepers in 1856 was 2,870, and in 1896 only 688. In 1885 a law was passed making the segregation of lepers compulsory, but it is understood that if a leper is able to provide himself with a separate bed, cooking and eating utensils, and have his clothes separately washed, he is not compelled to enter the leper hospital.

In Norway isolation is by no means absolute. The doors and gates of the hospital are not kept locked, and the inmates may sometimes be met in the neighboring roads, those who have no ulcerations being allowed to go out. They are kept in on market days. At Trondhjem and other places they are permitted to enter houses and churches or come in contact with other people.

In the island of Cyprus the effect of isolation is seen in the fact that previous to 1878 there were 150 lepers in the island, 120 of whom have been placed in the leper island; of these 57 have died and 63 remain. At the end of ten years there were not more than 30 lepers outside of the hospital, the whole number in the island not exceeding 100, showing a decrease of one-third during this comparatively short period (Thin).

In 1896 the British Government passed a bill to provide for the segregation of pauper lepers and the control of lepers following certain callings which extended to the whole of British India.

It is worthy of note that no person is termed a leper unless he is suffering from a variety of leprosy in which the process of ulceration has commenced, and the provision of the act extends only to a leper who has in a public place solicited alms or exposed or exhibited any sores, wounds, bodily injuries, or deformities with the object of exciting charity or obtaining alms. Such person may be sent to a leper asylum, where he shall be detained until discharged by order of the board.

The leper is prohibited from pursuing any of the following callings: (*a*) Practice as a medical practitioner, work as a barber, washwoman, water-carrier, baker, tailor, haberdasher, or domestic servant; (*b*) selling any food, drink, or drug for human consumption; (*c*) bathing at a stream or drinking at any drinking-fountain, well, tank, or reservoir; (*d*) riding in any public conveyance.

Violation of any of these acts is punishable by a fine not exceeding fifty rupees.

In the Straits Settlements a leper may be removed upon an order from the senior magistrate to the nearest detention ward or other building authorized for the reception of lepers.

A further act in 1897, entitled a warrant to amend the law relating to lepers, prohibits the leper from following any of the callings mentioned above.

Vagrant lepers may be sent to the leper asylum and detained until released by order of the Government.

A further provision of the same act makes it lawful for the commissioner to undertake the registration and visitation of lepers within the municipal limits. The landing of lepers is prohibited, and the master of a vessel from which such a leper is landed is liable to a fine not to exceed $500. Lepers unlawfully landed may be sent to the leper asylum or returned to the place whence they came.

In the Cape of Good Hope an act was passed in 1884 to "check the spread of the disease known as leprosy."

Any person suffering from "infectious" leprosy shall, after examination by the district surgeon and by another duly qualified medical practitioner, be removed to a hospital for lepers, therein to be confined according to the provisions of the law. This was amended in 1890, and infectious leprosy was defined as "leprosy in an advanced and grievous stage, whether embraced in the loss of any member of the body or any other mark of the disease." A distinction was made between such cases of leprosy as are advanced and likely to be of immediate danger to other persons and such cases as are less advanced, and separate provisions were made for dealing with cases of the one kind and the other. Indian immigrants and certain others afflicted with leprosy were to be sent back to their own country. Male and female lepers were to be entirely separated from each other while in the hospital. No communication or intercourse could be allowed between the persons confined in a hospital or location for lepers and persons not confined therein except the attendants of the hospitals, although the leper had the privilege of seeing his friends and legal advisers at reasonable times.

The leprosy law was amended in 1894, permitting any person or persons belonging to the family or relatives of the person about to be committed in the leper location to go with the leper, provided that in case of minors accompanying such leper the consent of the guardian or parent may be taken on behalf of such minors.

In 1892 a law was passed for the extermination and repression of the disease of leprosy in British Bechuanaland, which provides for the report of cases, the power of removal to the asylums, the creation of separate male and female asylums, and the power of removal to the asylum at the Cape of Good Hope.

In the Seychelles vagrant and pauper lepers may be removed to the leper asylum. It is lawful, however, to grant the application of

any next of kin or friend that such leper be delivered to such next of kin or friend and entrusted to his keeping.

The laws applying to Queensland, New South Wales, and other Australian settlements are practically the same. In addition the leprosy act of New South Wales (1890) provides for the obligatory notification of cases of leprosy; for the detention and isolation of lepers, the establishment of lazarettos, and other purposes. In Queensland the leprosy act of 1892 provides that when any case of leprosy or supposed leprosy is not reported by the medical practitioner under whose observation it comes, he shall be liable to a fine not exceeding £100.

In Jamaica there was a leper asylum law passed in 1896 which provides for the arrest of lepers wandering about begging and their consignment to the leper asylums. If the leper can furnish security for his proper maintenance and provide treatment, he may be discharged from the asylum.

The laws in regard to the employment of persons affected with leprosy are as follows: That he shall not be employed in the preparation or sale of any article which concerns the food, drink, or the clothing of the public in general, and shall not follow the occupation of a barber, washer of clothes, cigar and cigarette maker, tobacco manufacturer, or school teacher. Such person or the person who employs him shall be liable to a fine not exceeding £5, and in default of payment, to imprisonment with or without hard labor for a period not exceeding three months.

In the Leper Act for Barbadoes in 1890 there is provision made for the voluntary entrance into the leper asylum of any one suffering from the disease, and the compulsory entrance of those who seek alms or support or who are without any visible means of subsistence.

In the Islands of St. Christopher, Nevis, Antigua, Trinidad, and Tobago, the provisions of the different acts affecting leprosy are about the same. Lepers have the privilege of entering the leper asylums, and there is compulsory segregation of mendicant, pauper, and obnoxious lepers.

In British Guiana essentially the same provisions are made. Leper vagrants who are found wandering abroad begging alms, seeking pecuniary support, or exposing their leprous sores in any public road may be conveyed to the leper asylum. Lepers may be discharged on security being given for their treatment in private.

In Cuba and Porto Rico there are hospitals for the care of lepers, but entrance is not compulsory.

In the Island of Malta, the laws for checking the spread of

leprosy are to the effect that any person found, upon the examination of the medical board, composed of five physicians, three of whom shall be in the service of the Government, to be suffering from leprosy shall be removed to the asylum for lepers, to be there detained during the whole period of the disease. It is provided, however, that any person detained in the asylum may leave the asylum for the purpose of fixing his residence abroad.

In the island of Cyprus the leper laws of 1891 make various provisions for the isolation of all persons who are found upon examination of three qualified medical practitioners to be suffering from the disease of leprosy, in the leper asylum. Lepers may build separate dwellings for their own use within the precincts of the asylum grounds. There is a penalty of £5 for not giving information of the existence of lepers.

It will be seen from the section on "Geographical Distribution" that leprosy is very extensively distributed in almost all the French colonies. In New Caledonia it has been propagated with an almost incredible rapidity. The insurrection of 1878 contributed to disseminate the disease. In French Guiana leprosy "propagates itself with such rapidity that one-tenth of the population is infected." According to Jeanselme, Tunis, Senegal, the coast of Guinea, and the French Congo are all contaminated, but there are no accurate documents giving reliable statistics.

While numerous leproseries have been established in various parts of these colonies, strict isolation or segregation is nowhere practised. A decree of the French Government in 1840 decided that the situation demands the segregation of every free person who is attacked. A new decree was promulgated in 1841. It provides that "there will be admitted to the leprosery at l'Acarounay all persons diseased with leprosy who may make the demand, and that there will be sent there all those who, being recognized as attacked with leprosy, have no means of taking care of themselves." Persons in good circumstances who wish to be treated at home at their own expense may be isolated at a distance of two kilometres at least from Cayenne and one kilometre from villages. Unfortunately the provisions of the laws for the control of leprosy in the French colonies have never been strictly enforced.

In 1893 there was promulgated for New Caledonia a decree almost identical with that of French Guiana. These are the only French colonies where there has been established any regulation of leprosy.

The United States.—In this country the Government has taken no active measures respecting the prevention of leprosy beyond quarantine regulations with a view of preventing the immigration of persons

affected with the disease. These regulations promulgated by the Treasury Department through the United States Marine-Hospital service in 1894 provide "that vessels arriving at quarantine with leprosy on board shall not be granted pratique until the leper, with his or her baggage, has been removed from the vessel to the quarantine station. No case of leprosy will be landed. If the leper is an alien and a member of the crew, and the vessel is from a foreign port, said leper shall be detained at quarantine at the vessel's expense until taken aboard by the same vessel when outward bound."

Many years ago the people of *California* recognized the danger of the introduction of leprosy on the Pacific coast through Chinese immigration. Section 2,952 of the Penal Code provides: "It shall not be lawful for lepers or for persons affected with leprosy or elephantiasis to live in ordinary intercourse with the population of this State. But all persons shall be compelled to inhabit such lazarettos or leper quarters as may be assigned to them by the Board of Supervisors by the city or county in which they may be domiciled or settled. And the Board of Supervisors are vested with power and are required to make all necessary provision for the separation, detention, or care of lepers or persons affected with leprosy or elephantiasis settled or domiciled in their respective cities or counties."

Section 2,955 provides for the inspection of all persons arriving in California from foreign ports by the Commissioner of Immigration. Those found to be lepers are to be taken in charge by him and placed in a suitable lazaretto, and there detained separate from the general population so long as they shall elect to remain in the State, or until they shall have recovered, but they are allowed to return whence they came. The master or consignee of the vessel bringing lepers is liable to a penalty of $1,000 for failing or refusing to comply with the law.

Additional laws were passed in 1883, forbidding the landing of lepers from any ship, their transfer to another vessel, or their harboring by any person outside the lazaretto.

While there is ample legislation in California for the segregation of lepers, the health authorities in many towns are exceedingly lax about enforcing the laws.

In *Oregon* the health officers for the different ports are required to board all vessels arriving by sea and to examine passengers and crews for leprosy, but there is no provision for the detention and care of lepers.

Louisiana is the only State in the Union which has provided a home or asylum especially for lepers. In 1892 there was passed by the legislature "an act to prevent the spread of leprosy and provide

treatment for the same and for isolation of persons afflicted with said disease and penalties for non-compliance with the provisions of this act." This act was supplemented by one in 1894 which ordered that "all persons afflicted or suffering with said disease of leprosy shall be confined in an institution isolated and used for the treatment of said disease." Notification of all cases of leprosy was required under penalty of fine or imprisonment. Pursuant to the provisions of this act a home was established (1895) in Iberville Parish, about eighty miles from New Orleans. During the first year of its existence thirty-one lepers were transported to the home, twenty-three of whom were born in Louisiana. Since then a few additional cases have been admitted, but, owing to the apathy of the profession and the public, the provisions of the above acts have not been successfully carried out.

In *Massachusetts* the boards of health are empowered to isolate and provide necessary attention to persons afflicted with leprosy or other sicknesses dangerous to the public health.

The Board of Health of *New York* has, under the general provision of the chapter relating to diseases which in the opinion of the board shall be dangerous to the public health, the power to isolate leprosy. Several years ago the New York Board of Health began to take official cognizance of leprosy in this city. All lepers coming within their jurisdiction were isolated on North Brother Island. At first they were quartered in a tent on the island as far removed as possible from the other buildings. Later a cabin-like structure was erected for their confinement, from which they were transferred and quarantined in one of the disused buildings for contagious diseases. In 1897 the few lepers in confinement on North Brother Island were allowed to escape, and since then there has been no official action on the part of the Board of Health in reference to lepers in this city.

Many other of the individual States have made laws affecting the control of lepers within their respective borders, and the national Government exercises no jurisdiction over them.

There was passed January 24th, 1898, by the Congress of the United States, an act for the investigation of leprosy, which provides that the Supervising Surgeon General of the Marine-Hospital service, under the direction of the Secretary of the Treasury, shall appoint a commission of medical officers of the Marine-Hospital service to investigate the origin and prevalence of leprosy in the United States and to decide upon what legislation is necessary for the prevention and the spread of this disease. So far as can be ascertained no active steps have been taken to carry the provisions of this act into effect.

Hawaii.—In 1863 the health authorities became alarmed at the

rapid spread of leprosy in the Hawaiian Islands, and in 1865 the legislative assembly passed an act to prevent the spread of leprosy, which provided for the gathering together of all the lepers of the kingdom, with a view to their isolation and treatment. The execution of this act was entrusted to the Hawaiian Board of Health. A portion of land was set apart on the island of Molokai for the seclusion of the lepers, and a hospital for the reception and examination of the lepers was established at Kaliki, near Honolulu.

The method adopted by the sanitary authorities in dealing with leprosy is as follows: The authorities are empowered to bring all suspected lepers to the hospital for examination. The examination takes place under the supervision of the board of three physicians, who are selected for their especial fitness for this task. Those suspected of leprosy are kept under surveillance until either the suspicious symptoms have disappeared or unmistakable signs of leprosy are manifest. The pronounced lepers are kept secluded and forwarded to the leper settlement to remain there until they die.

Nearly all the lepers sent to the Molokai settlement have passed through the receiving station. In the earlier times some occasionally were sent there direct from other islands.

Since the establishment of the leper settlements over six thousand lepers have been received.

Geographical Distribution.

Asia.

India.—India has always been regarded as one of the chief and oldest centres of leprosy. It is exceedingly difficult to ascertain whether leprosy is on the increase or decrease, as in many districts there are no reliable data upon which to base an accurate estimate as to the prevalence of the disease. Vague and widely differing estimates have been given. According to the investigations of the commissioners of the national leprosy fund, who were sent to India to investigate and report upon leprosy, there were over one hundred thousand lepers in India. Little has been done in the way of legislation or in the systematic management of lepers; probably not two per cent. receive proper care. A leper asylum known as the Matoonga Hospital has been recently established near Bombay, with accommodations for three hundred inmates, entrance into which is voluntary. There are a number of other hospitals in which lepers may receive care and attention.

The census of 1891 gives 114,239 lepers in India, a proportion of 0.5 per thousand. There is in the presidency of Bengal 0.51 per

thousand; in Madras, 0.37 per thousand; in Bombay, 0.47 per thousand; in Lower Burmah, 0.63; in Upper Burmah, 1.18 per thousand; in Mysore and Coorg, 0.16 per thousand. In single districts, Bamkoora and Berhoom and Bengal, there are 3.63 to 3.52 per thousand. The island of Ceylon has about two thousand lepers—1.10 per thousand.

In certain regions leprosy is much more prevalent than in others. Dr. Van Dyke Carter found that from one-third to one-half of all the districts are affected with leprosy in variable proportions; in some the ratio was two lepers in one thousand inhabitants, and as high as one in two or three hundred people, or one in eighty, or even one in fifty existed in certain parts.

The opinion of the Leprosy Investigation Committee was to the effect that the available data point strongly to a decrease in the disease and that leprosy does not prevail in India to such an extent as to constitute a general or universal danger.

China.—Although China is one of the oldest and most prolific hotbeds of leprosy in Asia, it is impossible to obtain accurate statistics of the prevalence of the disease. The traditional policy of the Chinese, observed in their exclusiveness and their disposition to thwart outside investigation into their customs, habits, and manners of living; the enormous extent of their territory, much of it unexplored or unknown to modern civilization; and the teeming population (one-fifth of the human race), constitute conditions which preclude the possibility of obtaining accurate information. The general statement that leprosy prevails throughout the whole empire of China would seem to be contradicted by recent investigations.

Cantlie, in his prize essay on "Leprosy in China, Indo-China, Malaya, the Archipelago, and Oceanica" (New Sydenham Society, 1897), says that not one-third of the territory of China is under the ban of leprosy. It is certain that leprosy does not prevail in the north of China to anything like the extent it prevails in the southeastern parts. In endeavoring to arrive at the precise facts, based upon the most reliable data, it is necessary to compare the notes of various observers and carefully sift the evidence. For example, the statement was quoted in a prize essay of the national leprosy fund, by Dr. George Newman, that "at Tientsin there are two large asylums for wretches who are taken with leprosy, located on the outside of the city; two or three hundred lepers live at each of these asylums." Dr. Cantlie's investigations show that there are no leper hospitals at Tientsin.

Likewise it was stated by von Bergmann that Hanoi, the capital of Tonquin (one hundred thousand inhabitants), in Indo-China, was so

infected by leprosy that one-half of the inhabitants were lepers. The truth is that in the leper village not far from Hanoi one-half of the four hundred inhabitants were lepers.

In the province of Shantung there are a few lepers in almost every village, more in the interior than on the coast. In Hupeh and Szechuen leprosy is more or less prevalent. In the province of Fokien it is a veritable scourge.

The province of Kwantung is called by Cantlie the cradle of leprosy. In Kwantung there is a leper village near every large town in the province. There were formerly two leper asylums near Canton, one with seven or eight hundred inhabitants, the other over a thousand. At present there is but one leper village one and one-half miles outside of Canton with six hundred and fifty inhabitants. In addition to the lepers in this village several hundred dwell in the river on boats. In the district and port of Swatow, situated at the mouth of the Han River, which serves as a place of embarkation for the enormous coolie trade of the densely populated regions of this province, leprosy prevails extensively. In this district there are villages called leper settlements, but there is no segregation, and lepers are allowed to move about freely.

In Macau, a Portuguese settlement in Kwantung province, lepers are segregated on an almost inaccessible island, and the character of the coast acts as a natural barrier against leper deserters. They are not sent here until the disease is quite far advanced.

During Dr. Cantlie's visit there were in the leper island forty males and twenty-nine females. The proportion of Portuguese of the entire population affected with the disease would be about one per thousand.

The island of Hainan has a large proportion of lepers among its Chinese population. The aborigines are exempt.

In the island of Hong-Kong leprosy is more or less prevalent. In two and one-half years one hundred and twenty-five lepers presented themselves for treatment at the Alice Memorial Hospital. Before the annexation of the island by the British leper families and communities lived in huts on the hills about the town and maintained themselves by begging or otherwise. Since the British occupation, whenever a leper is suspected, the police arrest him, and if he should prove leprous he is sent away to the mainland. It is worthy of note, however, that a minimum calculation shows that in seven years, from 1880 to 1886, at least six or seven hundred lepers dwelt in the island of Hong-Kong unknown to the Government.

In the island of Formosa many of the Chinese population are lepers, but the Japanese are exempt. In the peninsula of Korea

leprosy is most prevalent in the south and dies away to the north. All the cases met with in the north are importations.

Dr. Cantlie says: "Leprosy in the far East is centred in the southeastern provinces of China. The coolie emigrants come chiefly from Kwantung and Fokien; three-quarters of the coolie emigrants from China are from these provinces, and the spread of leprosy in the Malay peninsula, in the Dutch, Spanish, and Portuguese East Indies, and in Oceanica, has been in all cases coincident and concurrent with the immigration and residence of coolies from these provinces. In no instance over this vast area has any native acquired leprosy except where Chinese coolies have settled."

The natives ascribe leprosy to the Chinese immigrants, and the name used shows the belief in the Chinese origin of the disease. There is no native name for the disease in the aboriginal languages, except in Malay.

The Chinese recognize thirty-two kinds of leprosy; the two principal forms, which they term "moist" and "dry," corresponding to the tubercular and anæsthetic types. The causes assigned for leprosy are almost innumerable. They believe in the hereditary transmission of leprosy, but believe that the disease does not go beyond the third generation. They attach a great importance to sexual intercourse in the spread of leprosy. In most provinces they think that the effluvia from the patient are sufficient to transmit the disease. When a leper quits his seat, another person will not hesitate to occupy it, but before the newcomer sits down he will fan the place where the leper sat as precaution against infection. The Chinese in some provinces believe that leprosy is caused by a microscopic animal which flies unseen. A person is stated to have been beaten with a stick smeared with blood from a leper, and to have died subsequently from leprosy. The urine tainted with leprosy is stated to have been the means of infecting healthy persons. Compulsory segregation is practised only by the Portuguese in Macau.

The methods used by the Chinese for the segregation of their lepers is by the establishment of asylums or settlements termed leper villages. Each asylum is under the control of a head man, who must reside at the institution and who is nominally or really a leper who manages the general affairs of the asylum, reporting from time to time to the district authority the condition of the establishment, admissions, deaths, etc. A small stipend is allotted to the lepers by the Government, which they supplement by begging in the streets, and thus eke out the means of a miserable existence. When a leper dies, his corpse is burned, as fire is supposed to destroy the insects which cause the disease. The leper villages are not isolation estab-

lishments, but merely refuges where lepers may dwell. The majority are beggars who daily go forth to obtain alms. They are met with in shops and streets, on the river, everywhere. These dwellers in the leper villages mix with the crowd, handle the food exhibited for sale, and pay the cash they carry in their leprous hands. Nobody refuses to buy from a leprous huckster, and provisions are bought fearlessly in the store of a leper (Ashmead). Cantlie says: "The leper village they dwell in serves merely as a hotbed of infection, and the disease will remain endemic so long as these nests of infection are maintained."

Cochin China.—Leprosy also extensively prevails in Indo-China, in Siam, Annam, Camboge, and in Tonquin. At the gates of Saigon at Tinghé there is, according to M. Jeanselme, a leprosery containing from two hundred to two hundred and fifty patients. At Tonquin leprosy is rare in the mountainous regions which are but little inhabited. The leprous village of Hanoi is situated in a depression. It is isolated by a high dike, pools, and impenetrable bamboo thickets. Half of its four hundred inhabitants are lepers. There is a smaller leper village in the city of Hanoi, and the leper mendicants freely traverse the streets of the capital. The disease is quite widely spread among the Annamites. Segregation is extensively practised. Lepers are not isolated in the villages, but live in separate localities from one another and take part in ordinary labor as if they were not diseased. In certain regions, however, they are segregated very vigorously. They are compelled to keep away from frequented roads and to follow special paths.

Malay Peninsula.—In Singapore, which is the headquarters of the British Government of the Straits, there is a large and well-appointed leper hospital. The inmates are chiefly Chinese, but a number of Malays, a few Portuguese, and occasionally some other European are met with among them. There is also a large leper asylum in Penang. Most of the cases are imported from other countries, principally China. Another leper hospital is at Johore. In all these hospitals the Chinese form the largest number of the patients.

In Perak leprosy is widespread, both Malays and Chinese being extensively affected. None of the Japanese are known to be lepers.

In Muar leprosy is uncommon. Chinese suffer mostly, Malays rarely.

Dutch East India.—In Malaysia leprosy has its principal seat in the islands of Java, Sumatra, and the island of Borneo, although other portions of the Dutch East Indies are infected.

Broes van Dort, as also Cantlie, insists that the propagation of the disease is especially due to the immigration of the Chinese.

There are in Central Java 30 to 38 patients; in Western Java, 42; in Eastern Java, 2,703; upon the east coast of Sumatra about 1,000; and upon the west coast, 156. In the island of Java the disease has taken on dangerous proportions. Up to 1865 there were fourteen hospitals. In 1886 there were six voluntary asylums for lepers. The inmates are principally Chinese, who are everywhere the chief sufferers. The few Europeans when attacked have returned to Holland. Since the introduction of European civilization leprosy is said to have increased, as formerly the Javanese killed their lepers or exposed them so that they should perish from lack of nourishment. The Malucca Islands and the Islands of Amunta and Tarnacte are also infected.

The Philippine Islands.—There are no data of a definite character accessible as to the prevalence of leprosy in the Philippine Islands. There are leper hospitals near Manila. One hospital in Luzon has one hundred and fifty beds. The general impression is that the cases which were the origin of local epidemics of leprosy in Valencia and Alicante, Spain, were imported from the Philippines.

Japan.—We have no knowledge of the origin of leprosy in Japan. The general impression is that it has existed in this country for centuries, at least six hundred years before the Christian era, and that the disease was formerly more severe in its ravages than it is now. According to the latest official communication, based upon the investigations of the Sanitary Bureau of the Home Office, there were in Japan (in September, 1897) 23,647 lepers distributed through the empire. Leprosy is more prevalent on the coast than in the mountainous regions of Japan. There is no attempt at government control of leprosy, and leprosy asylums or hospitals have never existed. In many instances the families themselves have a separate room for the leper member. People regard the disease as hereditary and do not marry members of a leprous family. The lepers intermarry among themselves.

Australia.—There is no official record of leprosy in any part of the Australian continent prior to 1885. Dr. Ashburton Thompson, in his contribution to the "History of Leprosy in Australia" (London, 1897), gives a chronological summary of all cases of leprosy in Australia which had been recorded. They amounted to 70 in New South Wales, 45 in Victoria, 48 in Queensland, 2 in Western Australia, and 19 in the Northern Territories. Of the New South Wales cases, 34 occurred among the whites. The large majority of the lepers in Australia have been Chinese and Kanakas (South Sea Islanders). The Chinese, however, are at present the most numerous.

There is no record of leprosy among the aborigines in any ex-

plored part of the continent before the known advent of emigrants with recognized leprosy; but that they are susceptible to the disease has been proven by the breaking out of leprosy among them since 1892. Dr. Thompson's table shows a general increase of recorded cases subsequent to 1877. It also shows a marked increase of cases subsequent to legislation for the control of leprosy in these colonies. For example, in thirty-one years before compulsory notification was established there were in certain districts seventy-two cases; in four years after compulsory notification sixty-three cases were recorded. He thinks that there is probably no such increase as would appear from these tables. The proportionately larger number which have been recorded within the last few years is due to the greater attention which is given the disease. The most stringent laws extant against leprosy have been enacted in Australia.

In *New Zealand* many cases have been discovered among the Maoris; both Chinamen and whites have also been affected. The disease is said to be declining.

In the *Samoan Islands* leprosy has been introduced within recent years, but its spread has been comparatively restricted.

In the *Fiji Islands* one per cent. of the inhabitants are lepers. Of twenty-one cases reported by Dr. Corney, eleven were in Indians; the others were in natives of other islands, Solomon, Tonga Islands, but there were no cases among the Europeans. The increase of leprosy in the Fiji Islands of late years has been attributed to the abolition of the practice of privately killing affected persons, which was in vogue before the British rule.

New Caledonia is one of the most important and extensive of the modern centres of leprosy. The disease is said to have been brought in by the Chinese, although its introduction may possibly have been through other sources. A Chinaman in 1866 or 1868 had been received by a tribe of Kanakas with whom he had lived for several years. His body and extremities were covered with hideous sores. Within ten years, according to the missionaries, several analogous cases were observed among the natives who had been previously exempt from the disease. In 1880 five New Hebrides islanders were found to be suffering from the disease, and in 1883 numerous lepers were found on the north coast of the island.

After the insurrection of 1878 and the dispersion of the tribe the malady was propagated with astonishing rapidity through the entire colony. It is estimated that at least four thousand Kanakas have been affected with leprosy in New Caledonia. In 1886 ten foreigners had contracted the disease; three years later forty-six had been attacked; and this estimate Dr. Grall says is much below the actual

number. There are three leproseries provided for the patients, but there is no strict isolation. The lepers of this archipelago were segregated at the leproseries of the Marquisas Islands, which contain about four hundred lepers.

Northern and Central Asia.—Little is known of leprosy in Central Asia. From Northern China it extends up to Kamschatka and up the land of the Jakats. It is slightly prevalent in Siberia and also prevails among the Kouts. Smirnow stated that in the province of Vilinisk there were in 1891 seventy-seven lepers in a population of about seventy thousand.

In Persia and in Turkestan little is known of the facts in regard to leprosy, except that it prevails more or less extensively in certain provinces. According to Munsch, the proportion is about one per thousand and in some districts one per hundred among the inhabitants of Turkestan.

In Asiatic Turkey the disease exists in Syria, Arabia, Asia Minor. In Asia Minor, according to von During, the proportion of lepers is about one per thousand of the inhabitants.

Leprosy prevails in all Palestine. The principal centres are at Jerusalem, Ramleh, and Naplouse, near Jerusalem. The leprosery of Byr About Jesus Hilfe contains about thirty-four patients. Another small hospital has six or eight inmates. The total number of lepers in Jerusalem is said to be forty to fifty. The Arabs are the principal sufferers, the Christians and Jews being comparatively exempt. The patients rarely enter the asylum in the earlier stage of the disease, but remain with their family and friends until they become helpless.

Africa.

Egypt has always been regarded as one of the oldest centres of leprosy. The official census which was made by Engel gives as the result a total of 2,204 lepers in 1893. This number is evidently very much below the exact figure. The disease is encountered principally in the delta and in the Upper Nile regions. The present Khalifa, according to the press reports, is suffering from leprosy, contracted by taking the wife of an emir who died of leprosy. It is met with in Abyssinia, in Darfur, and along the east coast line of Africa.

It is found in Madagascar, Mauritius, Isle of Réunion, Santa Maria, and in the Seychelles. In the island of Réunion there is a leprosery in which the number of patients varies between seventy and one hundred.

In *Madagascar*, according to Davidson, the disease has extended since the old laws of isolation were abolished.

In *German East Africa* leprosy prevails less upon the coast than in the neighborhood of the Great Lakes, where it is quite extensive, and in certain islands of the Victoria Nyanza. Here the Government established a leprosery (Metento), where, in 1895, 18 cases had been admitted. In South Africa leprosy for the past fifty years has shown a marked increase (Impey).

Cape Colony.—According to the most authentic records, leprosy existed among the earliest races which inhabited this continent. In South Africa, according to tradition, leprosy has always existed among the Bushmen. On account of the custom of the natives of abandoning their sick or driving them in the forests to die of hunger, the disease was kept in repression.

According to Dr. Isaacs, the Bantas, including the Kaffir tribes, with whom the earlier settlers came in contact in 1750, occupied a large part of the African continent. Leprosy was a disease well known to them and had existed as far back as their traditions went. They likewise had the custom of putting out of the way their sick and helpless.

The earliest official records of leprosy occur in the year 1756, during the Dutch rule. Early in the present century, in the year 1817, the first asylum for lepers was established by European missionaries at Hemel en Arde. Four hundred patients were admitted from 1817 to 1846. Later another asylum was established at Graf-Rinet. In 1846 the two asylums were closed, and the lepers transferred to Robben Island. In 1889 a compulsory segregation act was put in force, owing to the notable increase in leprosy. The total number of lepers admitted to Robben Island from 1846 to 1897 was 1,948. There are in Cape Colony at the present time 812 lepers; in Basutoland, 250 lepers; in Griqualand East and in the Transkeian district, 650 cases; in Bechuanaland, 10 cases; in Natal, 200 lepers; in the Orange Free State, 150 cases; in the Transvaal Republic, 105 cases.

German Southwest Africa is up to the present time believed to be free from leprosy. The disease is encountered in the Congo State, but not extensively. Most of the cases are met with in the lower Congo. It is unknown to the Kamerun; the estuary of the Niger seems to be also free from the disease, but it is found on the Gold Coast, Sierra Leone in Senegambia, and in the Canary Islands. Stamford, in *The Journal of Tropical Medicine* (No. 31), reports 15 cases of leprosy in the Canary Islands. Dr. Goldsmith estimates that in Madeira there are about 70 cases, or six to 10,000 inhabitants. There has been a sensible decrease in the disease in the past thirty years. Tonkin has never observed leprosy in the coast between Sierra Leone and Old Calabar. Lepers are found in vast numbers upon the

Upper Niger and along the Benin River. Leprosy also prevails quite extensively in Maroc.

Algeria.—Gemy and Raynaud report having observed 58 cases of leprosy in Algeria. Of these about 40 were in Algiers; the others lived at Constantine and other places. This number of cases reported is, in their opinion, very much below the actual number. The Spaniards brought the disease from Alicante and Valencia, in which region there exists a considerable leprosy centre. Some of the patients were afflicted with the disease at the time of their arrival in Algiers. In a great number it was manifest only after a residence of from three to twenty years.

Among the number there were 8 Jews, which represents a proportion of 1 per 1,000, as there are 8,000 Jews in Algeria.

EUROPE.

The countries of Central Europe have for the most part been free from leprosy since the decline and extinction of the great epidemic in the sixteenth and seventeenth centuries. Within the past two centuries only occasional cases have been met with here and there, and in these for the most part the patients have contracted the disease in foreign countries where leprosy is endemic.

Great Britain.—As a result of a careful and painstaking investigation Dr. Phineas Abraham, of London, reported to the Berlin Leprosy Congress that the total number of cases of leprosy of which he could find records in England, Scotland, and Ireland was 56, 14 of which were personal cases. He had reason to believe that there were about 20 more under the observation of medical men, who for various reasons were unable to furnish notes of their cases. Estimating a margin of about 20 unrecognized cases, he concludes that the number of cases of leprosy occurring during the last ten years in Great Britain and Ireland does not exceed 96, or certainly not more than 100. He concludes that there is no reason to believe that there are more lepers in the United Kingdom now than for many years past.

Jonathan Hutchinson, who sees more cases of rare diseases than any other man in London, says that "cases of leprosy are fewer now than formerly." All of the cases above mentioned contracted the disease in India and in countries where leprosy is endemic. The only cases recorded in this century in which the disease must have been communicated in England are the cases of Dr. Hawtrey Benson and Dr. Liveing, and a case published in Guy's Hospital Reports for 1868. From time to time supposed cases have been reported which

upon investigation proved to have been examples of erroneous diagnosis.

Holland, Belgium, Denmark, Switzerland, Germany, and *Austria* are practically leprosy free. In Holland there are 30 cases (Broes van Dort); in Belgium there are 4 cases (Bayet); in Denmark there are from 1 to 3 cases (Ehlers); in Switzerland there are 2 cases (Jadassohn); in Germany there are 33 cases (Blascho).

In *Germany* there has been noted within the past few years quite an epidemic around Memel, a village near the Russian frontier, supposed to have been brought in from the province of Cracow, in Russian Poland. The epidemic which began in 1873 has attacked 32 persons; of these 16 were imported and 16 acquired in the locality in which the patients live. Nineteen of the lepers have died. The Memel epidemic is regarded by leprologists as affording an admirable opportunity for studying the direct contagiousness of leprosy—brother to sister, daughter to mother, mistress to servant, servant to mistress, etc.

In *Austria-Hungary* the disease is sporadic in Bosnia and Herzegovina. The official report states there are 133 lepers, which number is, according to the reporter, vastly below the actual number.

In *Montenegro* about 1,000 to 2,000 of the inhabitants have the disease. Almost the entire Isle of the Vulcrans is infected.

In *Servia* and *Bulgaria* there are only a few cases reported (104 tubercular and 29 anæsthetic cases), but the indications are that the disease is quite prevalent.

Roumania.—Drs. Petrini and Kalindero reported to the Leprosy Congress the existence of 208 lepers in Roumania. The first record of its existence was in 1874. It has markedly increased since the Russo-Roumania-Turkish War in 1877. The greatest number of lepers are found along the roads followed by the Russian army or in the neighborhood of those roads.

Constantinople.—Von During reports that he has personally observed 258 lepers and estimates the entire number in the city at between 500 and 600. Zambaco Pacha estimates that there are 4,000 lepers in the Ottoman Empire. In Constantinople the Jews are the principal sufferers. The Mussulmans are rarely attacked, their immunity being attributed to their mode of living.

Greece.—Bergmann estimates the number of lepers upon the Grecian continent at about 400. Zambaco Pacha gives a similar estimate. During the war Greece received a large number of lepers from Crete, augmenting the number. The statistics of leprosy in Greece presented to the Berlin Leprosy Congress differ somewhat. Rosolimos estimates there are 99 lepers; Mitaftsis estimates there are 119 lepers.

Samos and other islands of the Ægean Sea are also infected. Ehlers found 15 patients in the peninsula of Pelion in 1897. He remarks that when one searches for lepers one always finds more than are upon the official lists.

Island of Crete.—According to Zambaco, Crete itself contains from 2,000 to 3,000 lepers. There are no reliable data to show when leprosy was introduced into the island. Dr. Smart in 1851–52 gave the number of cases in the leper villages as 625. There is no leper hospital on the island, nor are the patients subjected to any government or municipal control. The fear of contagion alone compels a semi-separation of the lepers in the three leper villages situated just outside the three principal towns. In 1891 Dr. Bilioti estimated the number at 320 out of a total population of 300,000, the number of males far exceeding that of the females.

Italy.—There are no definite statistics as to the number of lepers in Italy, although Pellizari states that the number is large. Ferrari reported several years ago 152 cases in Sicily. Mazza has observed 20 cases in Sardinia. Breda has seen 24 cases at Commachio. Small foci of the disease are known to exist in various parts of Italy. The ancient leprosery of San Remo, which is regarded as the last remnant of the ancient leproseries in Europe during the Middle Ages, always contains a few lepers. Giovannini has observed at Turin since 1890 13 Piedmontese lepers. Pellizari states that these figures all fall below the actual number.

Lepers are found along the entire Riviera, both the French and the Italian Riviera. Jaja reports 18 cases in Apulia. Amicis reports 15 leprous families in the vicinity of Naples. The disease is scattered in small foci throughout almost the entire country. There are also lepers in the islands of Elba, Malta, and Gozzo.

Portugal.—Leprosy prevails extensively in this peninsula. Falcao collected statistics of 468 lepers, but this number is far below the actual number. He estimates that the actual number of lepers in Portugal is not less than 1,000. Small foci of the disease are scattered here and there; the most infected centre is Lisbon. There are special hospitals for lepers at Lisbon and at Cordova, but there is no attempt at isolation. These hospitals contain a small number of inmates, who are free to enter or leave as they wish. Falcao has since collected reports of 772 cases.

Spain.—M. Olivade estimates that there are from 1,000 to 1,500 lepers in Spain, 500 of whom have come under his personal observation. The disease prevails most extensively in Galicia, Asturia, and Andalusia, Granada and Catalonia. There is a leprosery at Granada and another at Seville, the latter containing 40 patients. Poucet has

recounted the list of lepers and the origin and spread of the disease in 1850 in the village of Parcent, and Zuriaga gives details of cases which he has observed to the number of 66. There were known to be in 1888 in the province of Valencia 69 lepers, and in 1893, 120.

France.—There are leprosy foci at Brest, Bordeaux, Marseilles, and Toulon. On the Mediterranean coast along the French Riviera small foci of the disease are found, and sporadic cases in Brittany. There are, according to Hallopeau, constantly from 160 to 200 lepers in Paris, all of whom have been infected in foreign countries. It is worthy of note that so far as known none of these patients has propagated the malady.

As regards leprosy in *Iceland*, opinions differ whether the disease was of ancient origin, brought by the Norwegians in settling the island in 874, or whether it was brought from Norway about the end of the thirteenth century with the return of the crusaders. Towards the middle of the sixteenth century leprosy had obtained such a foothold as to attract public attention, and four hospitals were erected in four quarters of the island. The smallpox epidemic of 1707 destroyed more than one-third of the population and with them the greater part of the leper families. In 1848 the leprosy hospitals were abolished. In 1889 Ehlers personally examined 102 cases; besides there were 42 patients living at too great a distance to be accessible; making a total of 144 cases. Ehlers in his second voyage to the island, in 1895, unearthed 13 more cases, making a total of 157. In 1898 he knew of 181 cases, and thought that the number exceeded 200. Recently (1898) a new leprosy hospital of twenty beds has been established in Iceland, and a system of obligatory notification and modified isolation has been instituted.

In *Finland* there are known to be 67 lepers. In 1807 the disease had increased to such an extent that it was determined to isolate the sufferers in order to prevent any further spread. A building was erected at the end of a small island in Lake Kitajarvi, and the lepers were removed thereto. In 1845 the hospital system was abandoned.

In *Sweden* there are known to be from 70 to 75 patients, of whom 30 are isolated; 36 live in the province of Helsingland and 15 in Dalarne.

The most important centre of leprosy in Europe in modern times is in *Norway*. Three leproseries have been established in Norway—the Lungegaards Hospital in Bergen in 1857; two others in 1861, one in Molde, and the other in Throndhjem. In a period between 1857 and 1895 there were admitted to these hospitals 3,400 lepers, while during the same period 5,053 new cases of leprosy appeared.

The total number of known lepers at the close of 1856 was 2,870;

at the end of 1895, 688. The following table gives at a glance evidence of the remarkable decrease in leprosy in the last forty years:

Year.	New cases.	Results.					Number living at home.
		Died.	Transferred to leproseries.	Cured.	Emigrated.	Total.	
1856	....	....	....	..	..	....	2,598
1856–60	1,157	668	585	7	30	1,290	2,221
1861–65	1,027	549	732	9	45	1,335	1,913
1866–70	979	498	573	9	47	1,127	1,765
1871–75	703	456	434	8	66	964	1,504
1876	116	88	79	1	6	174	1,446
1877	110	78	92	1	7	178	1,378
1878	105	61	61	6	8	136	1,347
1379	86	69	70	3	10	152	1,281
1880	75	66	96	2	7	171	1,185
1881	62	75	61	2	8	146	1,101
1882	72	52	37	1	7	97	1,076
1883	90	58	63	5	5	126	1,040
1884	62	76	50	5	2	133	969
1885	74	77	63	17	3	160	883
1886	53	64	78	9	9	155	781
1887	53	37	50	1	3	91	743
1888	41	43	52	4	1	100	684
1889	42	34	54	7	12	107	619
1890	49	57	49	5	2	113	555
1891	23	45	45	4	2	96	482
1892	35	36	25	5	2	68	449
1893	17	45	24	6	1	76	390
1894	14	26	15	4	3	48	356
1895	14	26	17	5	1	49	321
Total	5,053	3,279	3,400	126	287	7,092	

It is known that 287 of the lepers emigrated from Norway, and of these about 170 went to North America. It is probable that the statistics of leper immigrants here given by Hansen are very much below the reality. Hansen believes that the only possible explanation of the remarkable decrease in Norway is that the segregation of so many lepers has prevented them from infecting their fellow-beings. He further believes that the most effective remedy to prevent the spread of leprosy is the isolation of as many as possible and preventing them from infecting others.

Russia.—Alarmed by the obvious increase of leprosy in Russia, the Russian Government ordered in 1895 a general census of leprosy in its dominions. Twelve hundred and ninety-nine cases were reported, and upon examination of these 1,200 were declared lepers. In 1889 it was calculated that there were from 1,500 to 2,000 cases in Russia, and that the number was increasing. In 1877 Dr. Walsh found 378 lepers in the Baltic province, 3 cases at Moscow and at St.

Petersburg. In South Russia, the Volga districts, the Crimea, the Don Cossack territory, and in Turkestan Professor Munch collected information of 373 cases. He believes that the Crimea serves as the starting-point for leprosy in Southern Russia, and particularly in the Don Cossack territory. Crimea was colonized in the thirteenth and fourteenth centuries by the Genoese, who brought leprosy with them. In some settlements the number of lepers is from 1 to 300, to 1 to 1,000 of the population. Such centres of leprosy have intervening healthy settlements or they are in communication with each other and then occupy a considerable extent of territory with several nests of the disease.

South America.

The western coast of South America is practically free from leprosy. Middendorf during twenty-five years' practice in *Peru* saw only three patients—two Chinese and one European.

Upon the north coast the disease is frequent in *Venezuela* and in Guiana. In Surinam alone there are from five hundred to two thousand lepers.

Leprosy also prevails in *Curaçoa*, St. Martin, and St. Eustatius.

Leprosy was probaby imported into *Brazil* in 1644 by the Portuguese. In the year 1697 there were so many lepers in Brazil that a special hospital was asked for in which the lepers might be treated. During the last two centuries it has spread throughout the country. There are special leper hospitals at Pernambuco, San Paulo, and Rio de Janeiro, although residence is not compulsory and no obligatory notification of the disease is imposed upon physicians. The entire coast of Brazil is affected. The last census has given the number as five thousand, which, according to Lutz, does not indicate one-half of the real number.

In *Uruguay*, Canabal reports that there are only twenty-seven lepers.

The disease exists likewise in the *Argentine Republic*. Since 1892 there has been noted a progressive increase in the number of lepers admitted into the hospital for infectious diseases at Buenos Ayres. Gache declares that the disease is frequent and increasing in the interior of the country.

British Guiana.—Leprosy was introduced into British Guiana by blacks from Africa. In 1831 the government report showed a total of 431 lepers. In 1841 there were 65 lepers. A general leper asylum was opened at Mahieia in 1858. During twenty years from 1858 to 1878 there were admitted into the hospital 1,120 patients, 879 males and 223 females. The present population of British Guiana is 278,-

000, and the ratio of lepers is estimated to be 1 in 4,276. According to another estimate there are more than 1,000 lepers in this country.

French Guiana.—In this country, according to Lauré, one-tenth of the population is infected. The disease was imported by the blacks from South Africa. The native Indians are absolutely exempt. At Cayenne the number of lepers is between 100 and 120.

Colombia.—The first authentic case of leprosy in Colombia was that of one of the Spanish governors who died in Bogota in 1646. Leprosy was unknown among the Indians previous to that period. The disease extended slowly during the next two hundred years, but in the last two or three decades the increase has been very rapid. Nearly all districts where leprosy was previously unknown have been invaded, and now nearly every locality in Colombia is more or less infected. The number of lepers in Colombia is not positively known. The number forty years ago was estimated at 400; at present it has increased to 27,000. A still later estimate gives the number at not less than 30,000. In the three hospitals provided for the reception of lepers there were in 1896 only 841 patients.

The West Indies.

Jamaica.—The consensus of opinion is that leprosy was brought to the West Indies by negroes imported as slaves from the west coast of Africa. The first official recognition of the disease was in 1865. In 1891 there were 85 inmates of the leper home in Kingston. The number of lepers at the date of the last report of Dr. Donovan, was 450, or 1 in 1,555 of the total population. Donovan thinks that many have not been recognized.

Trinidad.—The government census returns show that in 1871 there were 102 lepers, 93 per 1,000; in 1881 there were 149 lepers, 97 per 1,000; in 1891 there were 225 lepers, 112 per 1,000. These returns are not accurate, as the census ordinance made no provision for obtaining information concerning lepers outside the leper asylums.

There was no accurate census of lepers in Trinidad until 1889, although the number was variously estimated from 480 to 860. The census of the island in 1889 showed there were 348 lepers, 210 of whom were in the asylum; 43.56 per cent. were coolies who had the disease when they arrived from India, and about 38 per cent. were natives of the colony. In December, 1896, there were 218 inmates of the asylum. The disease appears to be on the increase.

Leeward Islands.—The census of 1891 gives the total number of lepers at 172.

In St. Christopher or St. Kitts the number has increased from 72 in 1872 to 120 in 1890.

In the island of Antigua there were, in 1891, 45 cases, 34 being in the asylum.

In both islands the percentage of lepers to the total population has doubled in the last twenty years.

French Antilles.—Leprosy is extensively spread in the French Antilles. At Guadeloupe and Martinique there is 1 leper to every 600 inhabitants. According to M. Brassac, the number of leper inmates of the leproseries of the two colonies on the island of Desirade is 100.

In the *Danish Antilles* there are at least 22 at St. Thomas. Santa Cruz possesses a small asylum for lepers, but entrance is not compulsory; they go and come as they please. Their present number is 82, 36 men and 46 women.

In *Cuba* and *Porto Rico* the disease prevails extensively. There are usually about 80 lepers in the San Lazaro Hospital of Havana. There are other hospitals in Santa Clara and Puerto Principe. Confinement in none of these hospitals was, under Spanish rule, compulsory, nor was the isolation of the inmates complete, as they were always allowed to go out during certain hours without any restrictions on their movements. Under American rule the sanitary authorities of Havana have ordered the sequestration of all lepers in the city, and the same regulations have been ordered at Santiago. The total number in Cuba has been estimated at from 300 to 500, which is probably below the reality.

In Porto Rico there are numerous lepers, but there are no statistics showing the actual number.

Barbadoes.—The increase of leprosy in the island of Barbadoes is shown by the census of 1871, 96; 1881, 108; 1891, 156. The ratio of the increase of leprosy to the increase in population in the last ten years has been from 57 to 80 per 1,000. There were 114 cases in the lazaretto at the last report.

St. Vincent.—The census returns of 1891 give 62 lepers, an increase of only 5 since 1881. In the asylum there were, in 1894, 23 cases, as against 19 in 1887.

Santa Lucia.—The census of 1891 gives 32 lepers. In Grenada in 1891 there were 21 cases according to the census; in the census of 1881 there were only 3 cases.

CENTRAL AMERICA.

There are no authentic statistics of leprosy in the States of Central America. Numbers of lepers may be seen in Panama, and the

disease is also prevalent in Costa Rica, Nicaragua, Honduras, Salvador, and Guatemala. In the latter country attempts have been recently made to secure segregation of the infected.

Mexico.

There is every reason to believe that leprosy was introduced into Mexico by the Spanish, as Cortez established a leper hospital in the city of Mexico, and there is no record of the existence of leprosy before the arrival of the Spanish conquerors. The states of Michacan and Sinaloa are the main centres of leprosy. The states of Guanajuto and Jalisco and the adjacent districts of the adjoining states and the state of Guerrora in the north are all infected with leprosy.

Orvañanos states that there are about 30 lepers in the leper ward of the Juarez Hospital. The San Pablo serves the purpose of a general hospital and a hospital for typhus fever and other infectious diseases and also as a leprosy hospital. In my visit to the hospital in 1889 I found 11 cases of leprosy, almost all of them of the anæsthetic type. No attempt at segregation of the lepers is made by the authorities. Many lepers may be seen in the streets of the city, and their entrance to the hospital is voluntary rather than compulsory. The special leper hospital was abolished about thirty-five years ago. Statistics fail to show whether the disease has been on the increase or not since the discontinuance of any attempt to isolate lepers, but many Mexican physicians assert that the disease is gradually decreasing.

North America.

Owing to the geographical continuity of the British provinces of North America with the United States and the intimate intercourse between the inhabitants of the two contiguous regions, the history of the introduction and spread of leprosy in the United States and Canada may be considered together.

New Brunswick.—Little is known as to the origin and spread in New Brunswick. Since 1815 it has existed continuously among the French settlements near the Bay of Chaleurs in the Gulf of St. Lawrence. Leprosy first appeared in Tracadie, situated on the bank of the Gulf of St. Lawrence, at the mouth of Miramichi River. It was said to have been introduced by the French emigrants from St. Malo, in Normandy. It was not until a number of people had taken the disease that public attention was drawn to it, and a lazaretto on Cheldro Island, in the Miramichi River, was established in 1844. In 1849 the present hospital at Tracadie was constructed to take its place. Altogether about 150 cases have been admitted since the foundation

of the hospital. At present there are 23 inmates. The laws are not sufficiently stringent to compel the imprisonment of lepers at large, and there has been no notable increase in the yearly number of inmates in a long period.

Cape Breton.—A small outbreak of leprosy was discovered in 1892 upon the Island of Cape Breton. There were then 11 cases observed in individuals living in close contact. This number has since decreased to 6 or 7 cases.

British Columbia.—About ten years ago the existence of leprosy was observed among the Chinese residents of the British Pacific coast. In 1894 Dr. Graham, of Toronto, reported 7 cases, 6 of which were in Chinamen and 1 in a white man. The patients were kept in quarantine on an island near the City of Victoria.

The United States.

The heterogeneous character of the population of the United States, embracing representatives of so many of the nationalities of the old world, renders it probable that leprosy has been introduced into this country through many sources. France, Spain, Portugal, Norway and Sweden, Africa, and China, as well as Mexico and South America, have doubtless furnished contingents. The fact that the disease shows no tendency to an alarming spread, except on our Southern seaboard, notwithstanding the supply of infectious material from such diverse and numerous sources, but rather shows a tendency to die out with the death of the imported lepers, would seem to indicate that the soil of this country is not favorable to the germination and growth of leprosy.

The importation of leprosy in the United States may be traced to several distinct sources.

1. It was introduced into the Atlantic coast cities and the countries along the Atlantic seaboard from the West Indies, and probably Africa through the importation of slaves and intercourse through travel and commerce with the neighboring West India islands.

2. By leprous immigrants from Norway and Sweden into the Scandinavian colonies of Minnesota, Wisconsin, Iowa, and Dakota.

3. By the Acadian refugees from the British provinces of New Brunswick into Louisiana.

4. By lepers from Mexico into Texas and States bordering the Gulf of Mexico and the Rio Grande.

5. By Chinese immigrants into San Francisco and elsewhere on the Pacific coast.

6. By Hawaiian lepers in California, Utah, and other parts of the country.

In Boston, New York, and Philadelphia, and other large cities there has always been a variable number of cases of leprosy, made up from foreigners of the various countries where leprosy is endemic and of American sailors, soldiers, and civilians who have visited or resided in foreign leprous countries.

In New Scandinavia, embracing certain regions in the Northwestern States of Minnesota, Iowa, and Wisconsin, whose population is estimated to be over one million, made up largely of immigrants from Norway and Sweden, have been observed a certain number of lepers. Dr. James C. White, in his report to the Berlin Leprosy Congress, 1897, estimates that there were 168 leper immigrants who either had the disease when they left home or in whom it developed after they came to this country; of these, about 30 still survive. Investigations which have been recently made would seem to indicate that the number of Scandinavian lepers exceeds the figures which have been heretofore given. It is probable that the number is augmented by the arrival of new cases from time to time among the Norwegian immigrants.

Dr. Bracken says we have knowledge of 51 lepers who have resided in Minnesota, of whom 17 died during 1890; 34 have been added to the records since 1890, 29 from Norway and 5 from Sweden. The statistics of 168 known lepers above referred to could not have included more than 17 of this number of 51.

Dr. Bracken thinks that there must be at present a total of about 20 lepers in Minnesota, although Northwestern physicians, who should be qualified to judge, estimate that there are at least 50. He estimates that there are 60 lepers in the States of Wisconsin, Iowa, North and South Dakota, and 128 in other parts of the United States, making a total of 160 Scandinavian lepers in the United States at the present time. Another estimate places the number at 104.

Utah.—In 1889 I called attention to the fact that among the accessions to the Mormon population of Salt Lake City there has been a certain number of lepers among the Hawaiian converts.

California.—The Chinese population of our Western States is quite large—25,000 in San Francisco alone. There had been up to 1894, as estimated, 196 cases of the disease detected in the State, most of which have been reshipped to China from time to time. At present there are 26 cases of the disease known to exist in California; a number are confined in the pest house in San Francisco. Among the inmates of the pest house there have been quite a number of Hawaiian lepers, who have come to this country either for treatment or to escape the rigorous laws of sequestration which exist there.

Oregon.—In this State a number of cases have been observed, principally among the Chinese residents.

South Carolina.—Turning now our attention to the Atlantic seaboard, we find that a limited focus of the disease was reported by Dr. Geddings as occurring in South Carolina, near Charleston, between 1847 and 1882. Sixteen cases have been observed during that period; according to the latest reports four of these patients still survive.

Florida.—The proximity of Florida to the infected West India islands renders the importation of the disease extremely easy. During the last ten years the number of lepers in Florida has been variously estimated as from 6 to 100.

Texas.—I have had personal reports of three cases of leprosy in Galveston and a number in San Antonio. Most of these originated in Mexico or in Louisiana.

Ohio.—Two cases have been reported as occurring near New Lexington, Ohio. The opinion of medical men who have seen them is divided as to whether or not they are true cases of leprosy.

Louisiana.—The most important centre of leprosy in the North American continent is in Louisiana. Leprosy was introduced into this State by the Acadian refugees who were expelled from their homes in 1758 and who settled in Lafourche and the Tesche River districts, and it is also claimed that it was introduced into New Orleans from Martinique. It increased to such an extent that a hospital was founded in New Orleans in 1785. The disease gradually diminished, and the hospital decayed, and was finally abandoned in 1807.

No definite history of prevalent leprosy can be found until 1866, although that leprosy still existed during this period is evident from the records of the admission from time to time of cases in the Charity Hospital of New Orleans. The attention of the health authorities was not attracted to its increase until 1866, when it appeared in Vermilion Parish, in a woman whose father came from Southern France. She died in 1870, and subsequently four children and a nephew became lepers. From this centre the disease has spread through several other districts in the State and infects both native-born citizens and the alien population. Dr. Jones collected a total of 37 cases from 1877 to 1880. In 1889 Dr. Solomon reported 6 cases in New Orleans. In 1883 Dr. Blanc reported 42 cases; in 1892 he reported 41 additional cases—83 altogether.

In 1894 Dr. Dyer reported 25 cases, and since then has reported 91, a total of 116. Most of the cases in New Orleans originated, according to Dr. Dyer, in the district near where the old leper hospital was situated. A lepers' home was established in Iberville Parish in 1895. Dr. Dyer's statistics embrace 277 cases—7 from 1800 to 1878; 270 cases from 1878 to the present day. Dr. Dyer reports that 171 pa-

tients were born in Louisiana, 8 elsewhere in the United States, and 39 were born in Europe. There was no instance of heredity and no patients who died under five or six years. One hundred and thirty-one patients are supposed or known to be living at the present time. The regulations for the compulsory isolation of lepers in Louisiana are not stringently enforced. No well-sustained measures for the control of the disease have been adopted. New cases are continually cropping up. At the moment of this present writing two new cases have just been discovered in St. John's Parish, both natives of the parish. Contagion has been traced to their association many years ago with an old leper who has since died of the disease, and in whose cabin they were frequent visitors.

Hyde, in his report to the Congress of American Physicians and Surgeons (1894) upon the "Distribution of Leprosy in North America," says: "It may thus be approximately determined that the cases of leprosy heretofore recognized in the United States have been distributed as follows: In Arkansas, 3; in California, 158; in Dakota, 2; in Florida, 6; in Georgia, 1; in Idaho, 2; in Illinois, 13; in Indiana, 2; in Iowa, 20; in Louisiana, 83; in Maryland, 4; in Massachusetts, 5; in Minnesota, 120; in Missouri, 2; in Mississippi, 2; in New York, 100; in New Jersey, 1; in Oregon, 3; in Pennsylvania, 6; in Utah, 3; in Wisconsin, 20—a total of 560." It is evident, however, from later reports that the number of lepers in this country is largely in excess of his figures.

Hawaii.

The position of the Hawaiian Islands and their maritime communication with so many countries where leprosy is endemic render possible the introduction of the disease from numerous sources. The history of leprosy in the Hawaiian Islands is somewhat vague. The understanding among the natives is that it was introduced by the Chinese, and it is always called by them the Chinese disease, "mai paka." The first case came to notice about 1848. The disease was known to be gradually spreading from 1855 to 1863, but the attention of the health authorities was not awakened to the alarming prevalence of the disease in the islands until 1863 when an act "to prevent the spread of leprosy," which provided for the gathering together of all the lepers of the kingdom, with a view to their isolation and treatment, was passed. In 1865 a hospital for the inspection and examination of lepers was built at Kalihi. In November, 1864, a portion of the island of Molokai was purchased by the Government. Within the first three months 174 lepers were sent to the

settlement. Since its establishment more than 6,000 lepers have been consigned to the settlement. The number of admissions from year to year varies according to the vigor displayed by the successive health boards in carrying out the provisions of law for the detection, arrest, and isolation of the lepers. In certain years, 1873, 1883, 1888, there was a notable increase in the number of lepers sent to the island, the number of 579 being sent in the latter year alone.

The following table which has been carefully compiled from the reports of the Hawaiian Board of Health shows the number of admissions, the mortality, and the number on the books at the end of each year from the establishment of the settlement to January 1st, 1898.

Year.	Admissions.	Deaths.	Discharged or unaccounted for.	Number on the books Dec. 31.	Year.	Admissions.	Deaths.	Discharged or unaccounted for.	Number on the books Dec. 31.
1864*	141	26	10	105	1882	71	121	6	649
1867	70	25	7	143	1883	301	150	15	785
1868	115	28	2	228	1884	108	168	8	717
1869	126	59	11	284	1885	103	142	26	655
1870	57	58	4	279	1886	43	100	8	590
1871	183	51	9	402	1887	220	108	4	698
1872	105	64	4	439	1888	579	212	28	1,035
1873	487	156	21	749	1889	308	149	7	1,187
1874	91	161	8	671	1890	202	158	18	1,213
1875	212	163	14	706	1891	143	212	2	1,142
1876	96	122	3	677	1892	109	137	19	1,095
1877	163	129	1	710	1893	211	151	..	1,155
1878	239	147	..	802	1894	128	155	3	1,124
1879	125	209	1	717	1895	106	128	15	1,087
1880	51	152	10	606	1896	146	116	2	1,115
1881	232	132	..	706	1897	124	139	..	1,100

* Settlement opened.

It will be seen from the above table that in the first twenty years of its establishment, to January 1st, 1866, there were 3,036 lepers admitted; in the next ten years, 2,049. In the first-mentioned period the number of lepers was from 200 to 800, the average being about 500. In recent years the number has varied from 1,000 to 1,200. This large excess is explained by the health authorities by the fact that they are now sent there at early stages of the disease. The average death rate of the lepers has been reduced from 20 to 25 per cent. to 13 to 15 per cent. Leprosy is by no means confined to the native population. In the first twenty years of the leper settlement, among the 3,036 admissions there were 22 Chinamen and 16 whites, about 1 per cent. With the past ten years the number of foreigners has averaged from 3 to 5 per cent.

The Chinese furnish the largest contingent of the foreign popu-

lation of the settlement. Among the nationalities represented are Americans, British, Germans, Portuguese, Spanish, Russians, negroes, South Sea Islanders, etc. It has always been the policy of the board to return to their own countries when possible the Chinese and Japanese laborers who become lepers. More than 100 cases of leprosy have occurred among the white population which are not included among the statistics of the leper settlement. Many foreigners learn the nature of their disease from their own physicians and voluntarily return to this country or Europe for treatment. The endemic of leprosy in Hawaii has afforded an excellent opportunity of studying the disease by competent medical men, enabling them to trace its origin and the influences of heredity, contagion, racial and other characteristics, food, climate, modes of life, etc., in favoring its spread.

In studying the geographical distribution of leprosy an attempt has been made to give the statistics of the disease in various countries, which have been compiled from the most reliable data accessible, and also the indications which point to an increase or decrease of the disease. It is to be understood, however, that these statistics are apt to be misleading, as indicating a number which falls far below the reality.

As regards the actual percentage of lepers in various countries, it is for obvious reasons an unknown and unknowable quantity. Any one familiar with the natural history of leprosy must recognize that it is impossible to compute the number of lepers in any country by the methods ordinarily used for the detection and registration of disease; only advanced cases are recognized by inspection. In every country where leprosy is endemic a large number of persons are infected months and years before it is known to themselves or to others. The disease exists in a latent state, but it is none the less leprosy.

Many of the above statistics are based upon the number of lepers in the hospitals or asylums provided by the government or health authorities. Only a small proportion of the leper community, and those probably paupers or advanced cases, enter these institutions. In many countries official cognizance is not taken of leprosy until the patients reach an advanced stage of the disease. In the government enactments for the control and suppression of leprosy in the various British colonies, the ordinance relating to leprosy thus defines the disease: "A leper means any person suffering from any variety of leprosy, in whom the process of ulceration has commenced." Again, "the term 'infectious leprosy,' is to be interpreted as meaning one who has leprosy in an advanced and grievous stage." Only pauper

lepers, unable to provide for themselves, come under governmental supervision. It is evident that in all these countries a large proportion of lepers, unless the disease is advanced and presumably infectious, do not come within the category of cases subject to segregation in hospitals or asylums.

The leper settlements are not a popular institution in any country, and a leper is not apt to present himself when he knows that his confinement is virtually a lifelong imprisonment. As a consequence, in countries where a strict policy of segregation is adopted lepers use every possible precaution to conceal all incriminating evidence of the disease, and when concealment is no longer possible they are often secreted and cared for by their relatives and friends. Again, the very severity of the measures necessitated by a rigorous policy of segregation is indirectly a cause of its partial failure. The severity of the banishment stimulates all the inventive resources of the patient to elude arrest. It is a matter of general knowledge that in Hawaii, where segregation is rigorously enforced, lepers hide themselves or are secreted by their friends, or they flee to the mountains and forests for concealment.

Another source of error arises from the difficulties which attend the diagnosis of the disease and applies with special emphasis to most countries where leprosy prevails to the greatest extent. In countries such as Europe and the United States and in the modern leprosy centres of Norway and Hawaii it would appear practicable to give facts and figures with approximative certainty and also to arrive at conclusions respecting the progressive, stationary, or retrogressive character of the disease which have a definite scientific value. This is obviously not the case in semi-civilized and Oriental countries, which are not under skilled medical surveillance. In many Oriental countries, such as Northern China, Japan, Thibet, the hill countries of India, and also Africa, we are compelled to rely largely upon the testimony or reports of native doctors, travellers, missionaries, and others who are unfamiliar with the characteristics of leprosy and who in most instances would be unable to recognize the disease when they saw it.

According to Dr. Murata, of the Investigation Bureau of Contagious Diseases (Tokio), quoted by Ashmead, the statistics of the Japanese Health Department give the total number of lepers in Japan at 23,660, but in Dr. Murata's opinion this figure could be doubled or trebled without exaggeration.

The inability to diagnose leprosy applies to many medical men, who may come in contact with the disease without knowing it, especially the anæsthetic form. Even in countries advanced in civiliza-

tion it is practically impossible to get accurate figures. Leprosy is not recognized on ordinary inspection except when the disease is advanced in its evolution and more or less disfiguring. There are many cases which are suspicious and not well defined, so that even skilled leprologists may hesitate or find it impossible to pronounce a positive diagnosis.

Norway and Hawaii have been instanced as countries in which it would seem possible to arrive at an approximately correct estimate of the number of cases of leprosy, since they are directly under skilled sanitary supervision.

In Norway the official count of the number of lepers in 1856 was given as 2,221. It has since transpired that the actual number at that date, verified by the deaths taken from the Bureau of Vital Statistics, was nearly one thousand more than was calculated.

Again, the statistics of leprosy in Hawaii are also to a certain extent misleading, although the method adopted by the sanitary authorities is systematic and well organized. There are about twenty government physicians established in the different districts of the various islands, one of whose important duties is to report all suspected cases of leprosy, and the police officers are empowered to bring every suspected leper to the Kalahi reception hospital for examination, and all persons who are pronounced lepers are forwarded by the next boat to the leper settlement to remain there until they die. The number consigned each year depends upon the more or less vigorous policy of the Board of Health and the activity of the agents of the board in identifying and apprehending the lepers.

In the report of the Hawaiian Board of Health (1890), we read (page 13): "According to the best information obtainable there are at the date of this report about one hundred persons supposed to be affected by the disease still at large who have not been before the examining board," and yet the statistics of the leper settlement during the next eight years shows that there were twelve hundred lepers sent to the leper settlement, or within the first five years seven hundred and ninety-three admissions. Now leprosy does not develop *d'emblée;* it may preserve its incognito for five or ten years, or even longer, before its identity is declared. It is probable that most of these twelve hundred persons sent to the settlement and many more not apprehended were lepers on March 31st, 1890, when the Board of Health reports that there were only about one hundred lepers at large.

One element to be considered in the calculation of the number of lepers is the vast number of cases of incipient, latent, or undeveloped leprosy existing in all countries where leprosy is endemic. These

cases may not be detected in the earlier stages, but they are none the less leprosy, and as the disease develops into a recognizable form they furnish recruits to the ranks of the leper population.

From these and other facts we must conclude that all statistics of leprosy in different countries are inexact, as they indicate a much lower number than actually exists. In the writer's opinion the figures should be doubled or trebled in order to arrive at the actual number of cases. In the same way the number of cases of leprosy in different cities, such as New York, Boston, Philadelphia, is largely underestimated. The writer has personally seen over fifty cases of leprosy in New York, without taking into account the number coming under the observation of other specialists.

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